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Original Communications

THE PRESENT CHAOS REGARDING RESECTION OF RESIDUAL CASEOUS LESIONS IN PULMONARY TUBERCULOSIS

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A FEW years ago, a somewhat generally accepted agreement on the indications for resection in pulmonary tuberculosis had been reached. Medlar's[1] excellent contribution regarding the residual caseous lesion and simple excision, however, started a wave of enthusiasm (prematurely) for resection of almost all residues remaining after chemotherapy treatment, regardless of the length of time it was used. This view still persists, in spite of the fact that investigators, including Medlar himself and his associates, now almost unanimously agree that we have no accurate evaluation of the pathologic and bacteriologic aspect of many of the lesions in question, nor any proof that they should be resected. Many lesions, including apparent scars, contain caseous foci. D'Esopo[2] states that while it appeared at the time Medlar's[1] contribution was made caseous residuals should be resected, the past two years of research prove this very questionable.

That the pathogenicity of tubercle bacilli may be affected by their accommodation to incarceration within the necrotic lesion is generally conceded. Acid-fast bacilli can be recovered from many of these lesions in smears and cultures. This is especially true of open, cavernous lesions, and to a much lesser extent in closed ones. Medlar[3] obtained positive cultures in only 7 per cent of the closed lesions and an average of 40 per cent in all specimens. Our findings corroborate this. However, the important question, whether many of these bacilli are virulent, is unfortunately still controversial in some quarters.

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Steenken[4] reported a few patients undergoing Isoniazid therapy, with positive sputum on cultures, which could not cause disease in guinea pigs. Many other investigators have tried to produce active disease from cultures and caseous material after continuous long-term chemotherapy and have failed. In Medlar's[3] few reported completed tests, guinea pigs inoculated with considerable material containing numerous bacilli failed to show evidence of disease six months after inoculation. In old apparently healed lesions many investigators think that the bacilli are dead, regardless of chemotherapy.

It must be remembered that the paper of Medlar and Welles and their associates,[1] which started the present resection scramble, was based on theory, not on proved evidence. Their opinions have mostly changed now regarding resection, but they believed in it then and presented the paper for discussion and further investigation. This has been pursued by research and medical men, as well as surgeons. It is unfortunate that further research was not done before surgeons began cutting with reckless abandon.

The question of which lesions to resect is not definitely established. There is a wide divergence of opinion on the subject. There are those who blindly follow Medlar's[1] unproved hypothesis and resect almost all residues with or without long periods of chemotherapy. Others, floundering in the maze of pathologic and bacteriologic reports of our researchers, are not sure of the pathogenicity of these lesions and are much more conservative. There seems to be no disagreement that open cavities are potentially most dangerous. D'Esopo states that cavities not closed in six months under chemotherapy usually never close under this regime alone, and that if cavities remain open, sputum, which may be negative for months, will again turn positive. We concur in this. Auerbach[5] has shown that, under chemotherapy, re-epithelization occurs at the bronchocavitary junction and often extends some distance into the cavity wall itself. The tubercle bacillus is an aerobic creature. A patent bronchial junction should add to the difficulty of causing it to die. It is difficult to understand how an open cavity can be sterilized unless complete epithelization occurs. Auerbach[5] believes that granulation tissue at the cavitary junction, before chemotherapy, causes a ball valve effect resulting in a ballooning of the cavity, and that these agents, which have greatest effect on surface lesions, clear the pathway and allow the cavity to reduce in size or close.

Why the contents of the cavity are not expelled, under these circumstances, is perplexing. Medlar[3] states these usually contain neutrophils which help liquefy the caseous material, and allow them to flow out. He[3] also agrees that in closed lesions the physiochemical environment is probably the reason bacilli here are apparently not virulent, but he thinks that it is only an assumption that unculturable bacilli are dead and not temporarily dormant. He and others suggest that new culture media and animals be used for experimentation. Dubos[6] states that long-chain fatty acids are powerful antimicrobial agents, and that these are released by lipolytic enzymes, during necrosis, with resulting caseous material. He also states that these fatty acids, and lactic acids in low

concentration are actually bacteriocidal. Before chemotherapy, it was thought that cavity closure, and healing resulted after the bronchial opening became occluded, rendering the closed inspissated material more susceptible to the physiochemical environment.

It is the small, nodular, apparently arrested residue present after one or more years of medical management, however, that is the most controversial. Canetti[7] concludes that dead bacilli exist, in these lesions, with or without chemotherapy. Sweany[8-10] believes their life under these conditions depends on the length of time they are imprisoned, and believes they are dead after five years. Mahon[11] states his studies show that streptomycin was rarely present in the center of the lesion, and that acid-fast bacilli found there could not be cultured. Murphy[12] questions whether we are justified in recommending even wedge resections in these lesions. Auerbach[5] says it is impossible to determine whether unobliterated residuals should be left in situ or resected. It seems incongruous to treat a hospitalized patient for twelve to eighteen months or more, watch the lesion clear from an extensive infiltration to a small residue that has remained stationary for months (with negative sputum for a year or more), and then debate whether to send him home or resect. (For brevity, the lesion just described will be referred to as a "nubbin" in this paper.)

That we see more filled cavities under chemotherapy is unquestionable, but this is difficult to correlate with Auerbach's findings. It is thought by some that chemotherapy, especially INAH, dries up the material and prevents its expulsion.

Many relapses or extensions of disease, before chemotherapy, obviously came from expelled caseous foci, but now this is not apparent. It seems from our experience that in a larger percentage of patients reactivation occurs in other lesions which previously existed. Examination of many serial roentgenograms seems to confirm this.

It has been our opinion that noncavernous lesions with somewhat extensively mixed residues after long chemotherapy, with little or no change in x-ray appearance, should be resected. We have no proof now, however, from bacteriologic studies, that even this is correct. Many feel that apparently thick-walled cavities should be resected early, but it is not controversial that cavity walls thin out markedly, under chemotherapy, and often become much smaller with walls so thin they are difficult to see. These lesions, with considerable assurance, can be expected to close and heal with some form of collapse therapy—pneumothorax, thoracoplasty, or phrenic added to their other therapy. Unfortunately, these procedures are now virtually obsolete, although there are many many thousands of individuals who have been made well and have remained so after their use. That these methods should be discarded, because in the past they were given with very poor indications and technique, is difficult to understand. It has been our thought that in filled cavities resection has seemed indicated; but again research does not confirm this theory.

The argument for widespread resection is that the patient's future would be less hazardous if all lesions including "nubbins" were removed. It is also

true, however, that a patient is better off with no surgery at all if he does not need it. This serious, painful, mental and physical experience should not be taken lightly. Deaths do occur from resection, as do bronchopleural fistulas, remaining lobes that fail to re-expand sufficiently, empyema, added thoracoplasty, Schede operations, as well as early and late exacerbations of disease. The percentage of these occurrences is small, and they are now less frequently encountered. However, it is 100 per cent in those who get them.

It is our belief that it is impossible, from roentgenograms or sputum studies, to know whether a small caseous area in the center of apparently firm, stationary, fibrous tissue is hazardous. We can rely only on the findings of investigators. Thinking of the extensive, caseous disease, which so frequently exists under thoracoplasty and knowing that the greater percentage of these patients lose their positive sputum, become well, and remain so, it is difficult to become excited over a "nubbin" encased in fibrous tissue. It frequently happens that more disease is found at operation than was apparent in the x-ray picture. Areas of so-called "satellites" often surround the "nubbin," and other infiltrations, not suspected preoperatively, show evidence of previous disease. After long chemotherapy, the former are now much less frequently observed. These areas, rather than the "nubbin" itself, may actually be the cause of reactivations after cessation of treatment. The surgeon does not remove all disease by wedges, segments or lobes, if disease has existed elsewhere previously.

Scars or "nubbins" are present in many thousands of people throughout the country, and most of them are, and have been, living normal lives for years. Nobody thinks of hospitalizing them, and resecting these lesions, unless reactivation occurs. Lesions, after long therapy, that still appear active or have open cavities are not discussed here. We are primarily concerned with the stationary, apparently healed "nubbin." Steele[13] reported about 10 per cent of his reactions for residuals proved to be unnecessary, but who can say what percentage of the remaining ones would ever reactivate? The length of chemotherapy treatment has been steadily increased. It is obvious that short-term treatment was unsatisfactory. If resistance does not develop, who can predict what the optimal period of therapy will be before considering resection or other procedures?

Since December, 1951, we have discharged over 600 patients after long-term chemotherapy for further ambulatory treatment in the out-patient department and have watched them carefully to date. Only eight have been rehospitalized. In this group there were 176 who had resection alone, 79 who had thoracoplasty, and 403 who had only chemotherapy. Three reactivations occurred in the resection group, none in the thoracoplasties, and five in those treated medically only. Two of the five without surgery showed no roentgenologic increase of disease, but were rehospitalized because of one or two positive sputums. These positive sputums have not been verified after long rehospitalization. The three reactivations after resections occurred in over-distended remaining lobes. It is too early to draw conclusions, but we present these figures for what they may be worth.

Continually changing chemotherapy programs have resulted in many interruptions of treatment. Our best results and fewer reactivations occurred in those who had its continuous long-period use. Most patients presented received streptomycin and PAS alone.

No one at this time can know definitely the exact status of resection in closed lesions. But, our researchers now inform us that it is very questionable they should be resected. They give their blessing only to its use in open cavities. Time and further research must tell us much more about its application in all residues. In the meantime resection of "nubbins" goes on with total disregard of the findings of investigators. It seems very probable that not much of anything is accomplished for the patient, except unnecessary invalidism, by this surgery. Reports of results following resection for these residues are meaningless for who can tell that these lesions would have ever caused future trouble if they were not disturbed?

The entire treatment of the caseous lesion at present is confusing and chaotic. When we are more enlightened, however, it seems that indiscriminate resection will be abandoned. Individual lesions will then, we hope, be given more intelligent management.

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DISCUSSION

DR. EDWARD S. WELLES, Saranac Lake.—I quite agree with Dr. O'Brien, and I think his paper has expressed perfectly the whole situation. I do not come here as an advocate or an apostle of resection. We presented a paper about small resections in 1951 before this Association at Atlantic City, reporting a small series of operations dating from January, 1950. We said at the time that this was a study, and that study is still going on and we could now report a much larger series of cases—which I am not going

to do, no figures, no statistics—and can only say that the percentages which Dr. O'Brien mentioned (and very thoughtfully did not show on the screen) agree very closely with ours. The number of recurrences after resection is very small, and the number of recurrences in a series treated with chemotherapy and then sent home when treatment was stopped with no resection is just about the same. So we do not know.

I have been interested chiefly in one feature of this question on which I might give Dr. O'Brien a figure; that is treatment of minimal tuberculosis. We have a small series over the years, and have now operated on between 40 and 50 patients with minimal tuberculosis and resected the lesions that we could find. Dr. O'Brien asks, "How do you know that those people did any better than if you had not resected them?" We have only one figure to go on; that is the statistics brought out by Dr. Robert Mitchell three or four years ago on minimal tuberculosis. Mind you, this is not moderately or far-advanced tuberculosis treated and brought back to a small shadow. This is original minimal. In a large series in over twenty-five years, 35 per cent of them relapsed; among the 40 or 50 patients we have treated so far, no single one has relapsed and I still think it is worth trying if that much improvement can be attained.

I congratulate Dr. O'Brien on presenting his chaos.

DR. JOSEPH GORDON, Ray Brook.—I should also like to express my appreciation of Dr. O'Brien's paper and tell you about four pegs that we are pinning up as a current concept for the indications for resection with combined chemotherapy.

First, enough experience has been gained thus far to indicate that the open cavity 4 cm. or larger fails to respond to combined therapy in a sufficient number of cases to make this, as a single measure of treatment, reasonable. These patients, on the other hand, are the ones from whom resistant organisms emerge, and we are ultimately obliged to try to salvage such patients in a poorer state when the chemotherapeutic agent is not nearly so effective.

Second, we recognize that there are certain patients who show rather marked toxic reaction to the drug relatively early, whose compensatory mechanisms, such as eyes and ears, neuromuscular, and cardiovascular systems, are originally impaired. They appear to show marked changes early, and should not be carried on a long-term chemotherapeutic program.

The third group, which is a relatively small one, but has the possibility of increasing as chemotherapy alone in unsuccessful cases goes on, is the group of patients who come to us with primary resistant organisms. In that group, of course, prolonged therapy, even with the addition of another agent, is not commonly successful, so that they might be approached relatively early with resection.

In the fourth group, lacking long-term follow-up data, includes the residual necrotic lesion that is perhaps 3 cm. in size or larger. We can draw on certain past experiences, as Dr. O'Brien has done with other forms of treatment. The solitary lesion under pneumothorax and under thoracoplasty often shows a good initial result, remaining negative in a fair number of instances. Others are seen to shell out with the result that a positive sputum and spread might occur. In such a group of cases, under chemotherapy, there is a reasonable prospect of the emergence of resistant organisms; therefore the patient will be handicapped as regards future treatment. Such foci then are best treated by resection despite the favorable chemotherapeutic initial result.

THE USE OF ISONIAZID AS A PROPHYLACTIC ANTIBACTERIAL AGENT IN PULMONARY RESECTION FOR TUBERCULOSIS

Preliminary Report

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INTRODUCTION

THE advent of antimicrobial therapy has widened the scope of pulmonary resection in tuberculosis. However, prolonged usage and injudicious application of these agents, especially streptomycin, have created limitations. These are manifested by postoperative complications due to the development of resistance by the tubercle bacillus. It became apparent that the hazards of surgery were increased when such a state did develop. Thus, patients were denied the surgical procedure which might well have returned them to a useful place in society.

The introduction of a new suitable agent for protection during excisional therapy was needed to increase the salvage rate in pulmonary tuberculosis. It follows that such an event would allow the prolonged use of streptomycin and para-aminosalicylic acid without fear of the development of resistant strains of tubercle bacilli to these agents.

Published results of the investigations as to the effect of Isoniazid (isonicotinic acid hydrazide) on experimental tuberculosis have revealed the following: (1) tuberculostatic and tuberculocidal action in vitro,[1] (2) marked antituberculous activity in vivo,[1, 2] (3) healing of progressive tuberculosis in guinea pigs caused by tubercle bacilli resistant to streptomycin and para-aminosalicylic acid,[3] and (4) low drug toxicity.[4, 5]

When the suppressive effect of Isoniazid on human pulmonary tuberculosis was demonstrated,[6, 7] it was felt that this drug warranted a clinical trial as a prophylactic antibacterial agent for pulmonary resection in tuberculosis. Accordingly, the following study was undertaken.

METHOD OF STUDY

Following the recommendation for pulmonary resection, the patients on the present series were accepted for Isoniazid therapy in consecutive order. No attempt at case selection was made.

A minimum period of two months from the time of operation was arbitrarily chosen to note the appearance of possible surgical complications while on Isoniazid therapy. The medication was commenced forty-eight hours prior to

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operation. It was administered orally in the dosage of 200 mg. per day or 3 mg. per kilogram of body weight. During the immediate postoperative phase when the patient was unable to tolerate oral intake, Isoniazid was given intramuscularly in the same dosage. It was then recommenced by the oral route at the appropriate time. The original plan included an attempt to diminish copious tracheobronchial secretions by instituting Isoniazid therapy two weeks prior to surgery. No such problem arose during the present interval of observation. However, consideration for this modification of drug therapy seems worthy, as the volume of tracheobronchial secretion has been noted to decrease during Isoniazid therapy.

The efficiency of Isoniazid was to be measured by the number and extent of postsurgical complications due to tuberculosis. Thus, the object of this essay is to answer the question, "Does Isoniazid afford adequate antibacterial protection during the operative period and for a minimum postoperative period of two months against the tubercle bacillus?"

PROCEDURE

During the interval from Oct. 13, 1952, to Jan. 26, 1953, twenty-six pulmonary resections were performed. The medication under discussion was used on these patients in rotation. Three of the above twenty-six were excluded from the series because they had received a previous course of Isoniazid. It was presumed that their tubercle bacilli were resistant to Isoniazid.

We are presently concerned with twenty-three operations on twenty-three patients. These patients ranged in age from 15 to 61 years. Of the twenty-six, twelve of the patients were women and eleven were men.

The indications for pulmonary resection in this group approximate that seen in the current literature. In general, the indications fall into the following patterns: (1) thoracoplasty failures; (2) residual disease after prolonged antituberculosis therapy; (3) negative sputum with residual disease, as noted by roentgenogram, which is not likely to remain stable; and (4) negative sputum, indeterminate pulmonary lesions.

It should be understood that the listed surgical indications apply only to the group under observation. They are not meant to represent a complete discussion of the criteria for pulmonary resection in tuberculosis.

PREOPERATIVE ANTITUBERCULOSIS MEDICATION

As would be expected the majority of the twenty-three had had antituberculosis medication before surgery. Twenty had received a minimum of one and a maximum of three courses of streptomycin and para-aminosalicylic acid. Within this group, two had received thiosemicarbazone. One patient, of the twenty-three, had received para-aminosalicylic acid alone. Two had not had any antimicrobial therapy.

STREPTOMYCIN SENSITIVITY

The tubercle bacilli of eight of the twenty-three patients were resistant to streptomycin. Three were completely resistant to 100 μg, two to 10 μg. Seven

of the streptomycin-resistant patients had received previous treatment with streptomycin and para-aminosalicylic acid. The exception was a young girl who probably was exposed to an open case of pulmonary tuberculosis which had been treated with streptomycin.

SPUTUM

The tracheobronchial secretion was considered to be positive* for acid-fast bacilli preoperatively in fifteen patients and negative† in eight. Of the eight negative sputum cases, two were indeterminate lesions preoperatively and the diagnosis was in doubt. In both of these acid-fast bacilli were demonstrated in the resected specimen. The remaining six patients were advised to have pulmonary resection because the stability of their lesions seemed unlikely, even though their sputum was negative.

OPERATIVE PROCEDURE

Operative technique is a secondary consideration in the present study. However, a few sentences will assist in clarifying the prophylactic objective sought by means of the use of Isoniazid. The classification of operations is:

1. Pulmonary resection	23
a. Pneumonectomy	1
b. Lobectomy	8
c. Lobectomy and segmental resection	5
d. Segmental resection	5
e. Subsegmental resection	4
2. Concomitant thoracoplasty	3
3. Resection under thoracoplasty	12

The primary aim in operative technique was to conserve as much parenchyma as possible. This principle involved dissection close to the palpable and visual residual disease.

PLEURAL CONTAMINATION

Bronchiogenic tuberculosis may begin as a segmental or subsegmental disease. It may soon lose its respect for anatomic boundaries. As the inflammation progresses intersegmental planes may be penetrated and passed. Thus, not infrequently portions of the adjacent segments need also to be excised.

While following the diseased process through the pulmonary parenchyma a suppurative area is easily inadvertently punctured. Therefore, while attempting to perform a segmental resection for disease that has partially involved an adjacent segment an escape of purulent material is not unlikely.

A critical observation was made for gross visible pleural contamination. If a drop of purulent material was spilled, the pleural cavity was considered contaminated. If in the severance of diseased tissue caseation necrosis was seen, the pleural space was likewise considered contaminated. Eleven of the twenty-three cases had gross pleural contamination. Unquestionably, if larger volumes

*Persistently or intermittently positive by smear, concentrate, or culture four months preoperatively.

†Negative by culture four months preoperatively.

of parenchyma had been resected, the incidence of pleural contamination would have been less. But, such action would have defeated the principle of pulmonary tissue conservation. These latter cases will be considered in more detail.

CASE REPORTS

CASE 1.—J. H., an 18-year-old girl, had never had a sputum positive for acid-fast bacilli. Preoperative therapy consisted of pneumoperitoneum, streptomycin, and para-aminosalicylic acid on a presumptive diagnosis of tuberculosis. A fibrocaseous nodule was resected from the apical segment of the right upper lobe. It contained acid-fast bacilli on smear, but they failed to grow in culture. A small amount of suppurative material contaminated the pleural cavity at operation. The postoperative course was uneventful, and the sputum has remained negative for acid-fast bacilli by cultural methods. The histologic diagnosis of the resected specimen was fibrocaseous tuberculosis.

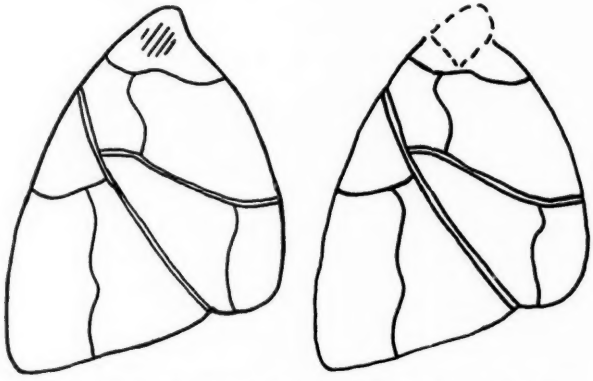

Fig. 1.—J. H. Age 18 years. There was pleural contamination. The diagonal lines represent fibrocaseous tuberculosis; broken lines, the resected parenchyma.

CASE 2.—I. C., a 48-year-old woman, had a persistently positive sputum for acid-fast bacilli. She had far-advanced bilateral disease. Preoperative therapy consisted of pneumoperitoneum, thoracoplasty, streptomycin, and para-aminosalicylic acid. The right lung with the exception of three basal segments was excised. Caseous material escaped when the medial basal segment was removed. The postoperative course was complicated by jaundice during the eighth postoperative week. This was considered to be homologous serum in type and she has recovered from it. The postoperative sputum is negative for acid-fast bacilli by culture. Histologically the lesion was fibrocaseous tuberculosis with cavitation, tuberculous bronchitis, and pulmonary fibrosis.

CASE 3.—T. K., a 23-year-old woman, had moderately advanced bilateral disease and a negative sputum. Preoperative therapy consisted of pneumoperitoneum, streptomycin, and para-aminosalicylic acid. The patient underwent an anterior segmental resection of the left upper lobe. Suppurative material contaminated the pleural space. Smear from this lesion was positive for acid-fast bacilli, but the culture was negative. Streptomycin resistance to 3 μg was present. The postoperative course was complicated by homologous serum jaundice. The sputum remained negative by cultural methods. The histologic diagnosis included fibrocaseous tuberculosis and tuberculous bronchitis.

CASE 4.—N. Y., a 26-year-old woman with a negative sputum, underwent a subsegmental resection of the posterior segment of the right upper lobe. Preoperatively pneumoperitoneum, streptomycin, and para-aminosalicylic acid were used therapeutically for minimal unilateral

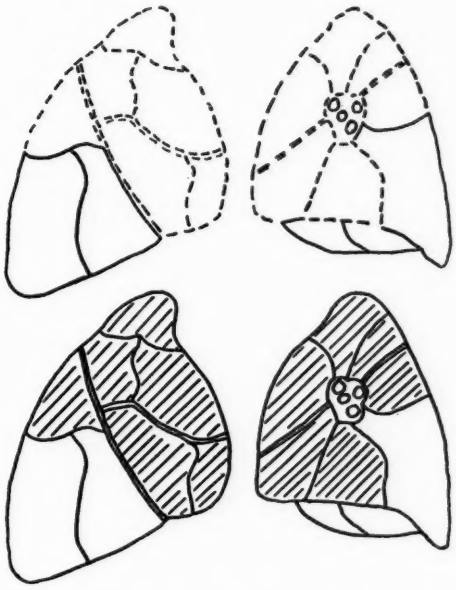

Fig. 2.—I. C. Age 44 years. There was pleural contamination. The diagonal lines represent fibrocaseous tuberculosis with cavitation, tuberculous bronchitis, and pulmonary fibrosis; broken lines the resected parenchyma.

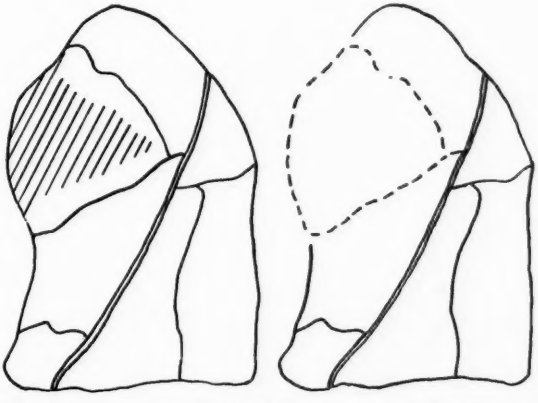

Fig. 3.—T. K. Age 23 years. Diagonal lines represent fibrocaseous tuberculosis and tuberculous bronchitis, broken lines the resected parenchyma. Pleural contamination occurred. The patient was streptomycin resistant (3 μg).

disease. Suppurative material from a blocked cavity escaped during operation. Histologically the disease was fibrocaseous tuberculosis and pulmonary fibrosis. The postoperative course was benign and the sputum remains negative to culture.

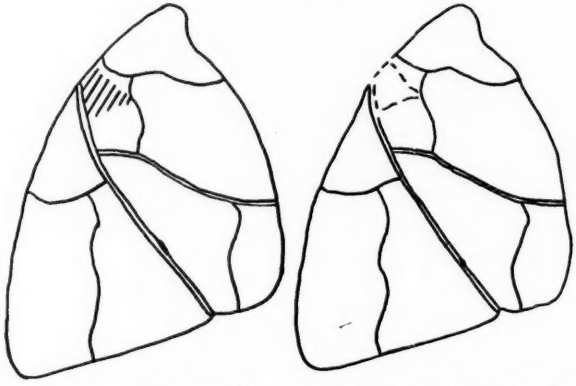

Fig. 4.—N. Y. Age 26 years. Diagonal lines represent fibrocaseous tuberculosis and marked pulmonary fibrosis; broken lines the resected parenchyma. Pleural contamination occurred.

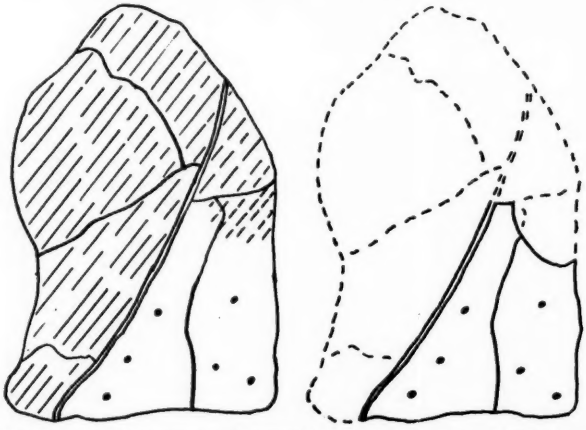

Fig. 5.—D. C. Age 46 years. Preoperative thoracoplasty. Diagonal lines represent airless lung with fibrocaseous tuberculosis; broken lines, the resected parenchyma; dots, scattered nodular disease. Pleural contamination occurred. The patient was streptomycin resistant (10 μg).

CASE 5.—D. C., a 46-year-old woman, had far-advanced bilateral pulmonary disease. The sputum was negative preoperatively. Therapy before operation consisted of pneumoperitoneum, phrenic crush, thoracoplasty, and several courses of streptomycin and para-aminosalicylic acid. Stretopmycin resistance was present to 10 μg. The left lung was excised with the exception of the basal segments. Suppurative contamination of the pleura occurred. Acid-fast bacilli were demonstrated in the contaminating exudate and grew on culture. Postoperative course was benign and the sputum remains negative to culture. Histologic diagnosis was fibrocaseous tuberculosis.

CASE 6.—V. P., a 61-year-old man, had diabetes mellitus. Sputum had been persistently positive for acid-fast bacilli. Preoperative therapy consisted of pneumoperitoneum, thoraco-

plasty, streptomycin, and para-aminosalicylic acid for unilateral far-advanced disease. The apical posterior and anterior segments of the left upper lobe and the superior segment of the left lower lobe were excised. Suppurative material escaped into the pleural cavity at operation. Postoperatively the patient's course was complicated by a persistent fever which responded satisfactorily to penicillin and Terramycin. The cause of this fever remains obscure. Sputum studies reveal the persistence of acid-fast bacilli. Histologically the lesion was fibrocaseous tuberculosis with tuberculous bronchitis and cavitation.

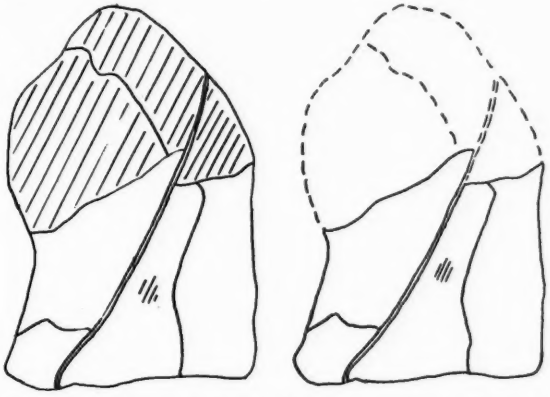

Fig. 6.—V. P. Age 61 years. Patient had diabetes millitus. Diagonal lines represent fibrocaseous tuberculosis with tuberculous bronchitis and cavitation; broken lines, the resected parenchyma. Pleural contamination occurred.

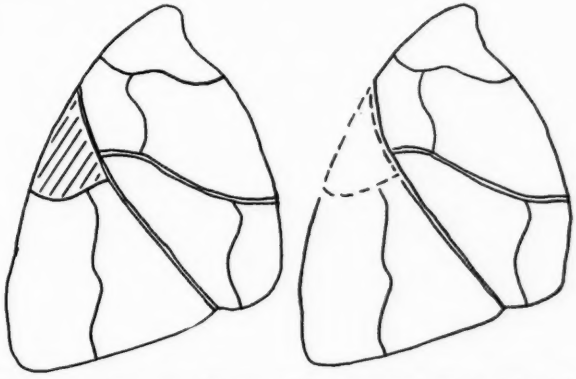

Fig. 7.—B. C. Age 18 years. Diagonal lines represent fibrocaseous tuberculosis and tuberculous bronchitis; broken lines, the resected parenchyma. Pleural contamination occurred. The patient was streptomycin resistant (100 μg).

CASE 7.—B. C., an 18-year-old girl, had minimal unilateral disease with a positive sputum. She had had no preoperative therapy yet the tubercle bacilli were completely resistant to streptomycin to 100 μg. A right superior segmental resection was done and a blocked cavity inadvertently opened. The postoperative course was marked by persistent fever and a local accumulation of fluid opposite the resected segment. The fever gradually subsided to normal under the influence of penicillin and Terramycin. The pleural fluid, as noted by a roentgenogram, is clearing. Sputum is negative to concentrate, but the culture has not yet been completed. Histologically the lesion is fibrocaseous tuberculosis with tuberculous bronchitis.

CASE 8.—G. G., a 32-year-old woman with a positive sputum, had an apical posterior segmental resection of the left upper lobe. Preoperative treatment consisted of phrenic crush, pneumoperitoneum, and para-aminosalicylic acid for unilateral moderately advanced disease. Caseous material was exposed at operation. The postoperative course was benign. Sputum studies show a negative concentrate, but the culture is not completed. The histologic diagnosis is fibrocaseous tuberculosis.

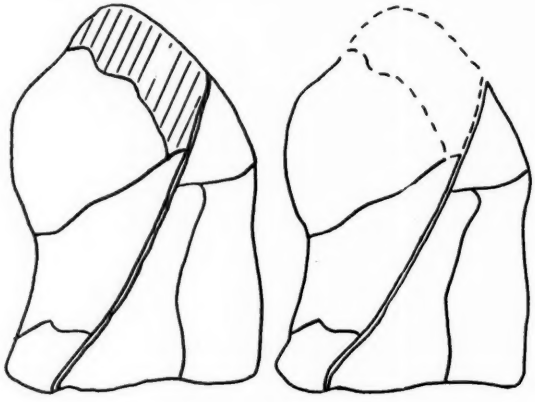

Fig. 8.—G. G. Age 32 years. Diagonal lines represent fibrocaseous tuberculosis; broken lines, resected parenchyma. Pleural contamination occurred.

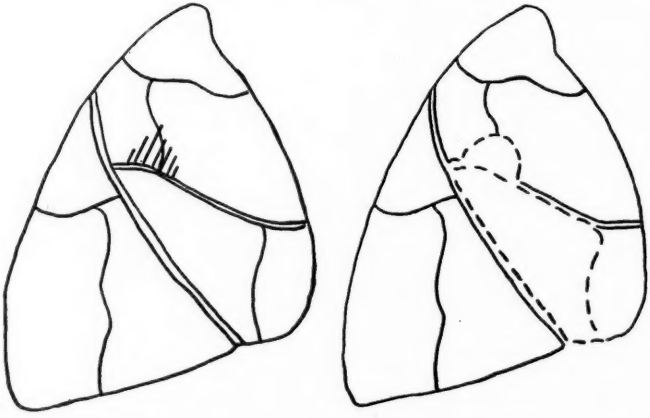

Fig. 9.—M. D. C. Age 31 years. Diagonal lines represent fibrocaseous tuberculosis with tuberculous bronchitis and cavitation; broken lines, the resected parenchyma. Pleural contamination occurred.

CASE 9.—M. D. C. This 33-year-old woman had a coincident condition of neurofibromatosis (von Recklinghausen's disease). She had far-advanced bilateral disease with a contralateral healed, mixed tuberculous empyema. Sputum had been persistently positive. Preoperative therapy consisted of a left pneumothorax, left thoracostomy, pneumoperitoneum, streptomycin, para-aminosalicylic acid, and thiosemicarbazone. A subsegmental resection of the posterior and anterior segments of the right upper lobe exposed the interior of a cavity. During exposure of the lesion through inflammatory tissue the bronchus to the lateral segment

of the middle lobe was compromised. It was necessary to excise this latter segment. The postoperative period was uneventful, and the sputum is now negative by culture. Histologically the disease was classified as fibrocaseous tuberculosis with tuberculous bronchitis and cavitation.

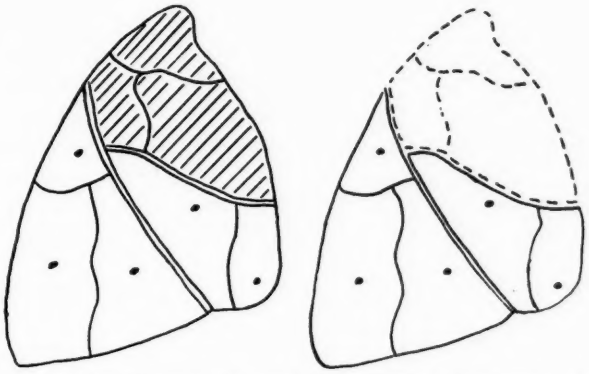

Fig. 10.—K. K. Age 23 years. Diagonal lines represent fibrocaseous tuberculosis with tuberculous bronchitis; broken lines, the resected parenchyma. The patient was streptomycin resistant (3 μg). Pleural contamination occurred.

CASE 10.—K. K. This 28-year-old woman had bilateral far-advanced disease with a persistently positive sputum. A cavity was opened during the process of a right upper lobectomy and concomitant thoracoplasty. Preoperative therapy consisted of pneumoperitoneum, streptomycin, and para-aminosalicylic acid. Streptomycin resistance to 3 μg was present. Postoperative phase was uneventful and the sputum is negative to culture.

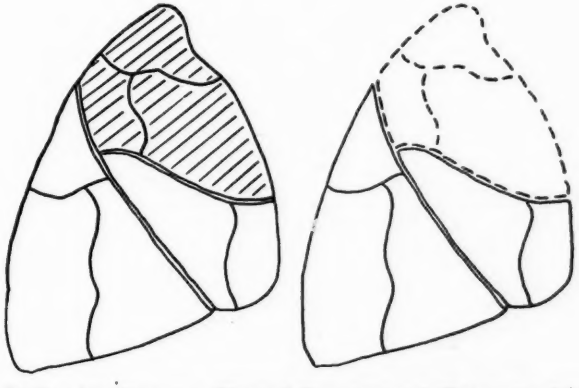

Fig. 11.—E. D. Age 31 years. Diagonal lines represent fibrocaseous tuberculosis with tuberculous bronchitis and miliary dissemination and chronic granulomatous pleuritis; dots, scattered nodular disease; broken lines, the resected parenchyma. (The concomitant modified Schede thoracoplasty is not shown.) The patient was streptomycin resistant (100 μg).

CASE 11.—E. D. This 31-year-old man had far-advanced disease which was bilateral. Also present was an ipsilateral, draining, mixed tuberculous empyema. Previous therapy consisted of pneumothorax, pneumoperitoneum, phrenic crush, thoracoplasty, cavernostomy, streptomycin, and para-aminosalicylic acid. Streptomycin resistance was complete to 100 μg. A right upper lobectomy and concomitant modified Schede thoracoplasty were done. The

lateral margin of the empyema communicated with the free pleural space at the end of the operation. Postoperative sputum is negative by culture and the empyema space is epithelized. Histologic diagnoses include fibrocaseous tuberculosis with tuberculous bronchitis and miliary dissemination, tuberculous sinus tract of the skin, and granulomatous pleuritis.

DISCUSSION

The clinical evaluation of a drug is difficult to perform with exactness due to the many variables and lack of complete control. However, certain trends become apparent. The fact that there were no complications attributable to tuberculosis indicates that Isoniazid did, indeed, play the role of a prophylactic agent.

The bacteriologic study of the resected specimens was commenced late in the initially described time interval. Of the twenty-three specimens, three were positive by smear and negative by culture for acid-fast bacilli, four were positive to both smear and culture, one was negative to smear with unfinished culture, and fifteen were not examined. Included in the group of positive smear and positive culture are specimens from the two patients who had not received preoperative streptomycin and para aminosalicylic acid.

No analyses or conclusions were attempted from such a small series. The apparent inconsistencies of smear and cultural examinations of resected lesions are well recognized. Medlar[9] speculates that these discrepancies are due to: (1) antimicrobial therapy resulting in dead organisms, (2) biochemical properties of the necrotic lesion resulting in dead organisms, and (3) insufficiently sensitive cultural methods.

Bacterial resistance to Isoniazid develops in approximately two to three months.[10] After resistance has developed, it is likely that the prophylactic antibacterial effect would be greatly diminished or lost. However, that was neither proved nor disproved by the work in this study.

Following the pattern of streptomycin, it is becoming increasingly difficult to find a patient who has not had a course of Isoniazid. Such a state may jeopardize the future of patients needing a pulmonary resection. It is suggested that Isoniazid be withheld from cases in which a pulmonary resection may be necessary in the future.

RESULTS

Twenty-three pulmonary resections for tuberculosis were completed on twenty-three patients.

TWENTY-THREE PULMONARY RESECTIONS

Postoperative nontuberculous complications	5
Homologous serum jaundice	2
Chest wall abscess	1
Local accumulation of pleural fluid	1
Persistent fever, unknown origin	1
Postoperative tuberculous complications	0

There were no bronchopleural fistulas, no tuberculous empyemata, no contralateral spreads, or reactivation of previously quiescent disease. In one case, the contralateral active disease improved as noted by roentgenogram.

CONCLUSIONS

The question asked earlier in the discussion, "Does Isoniazid afford adequate antibacterial protection during the operative period and for a minimum postoperative period of two months against the tubercle bacillus?" may be answered in the affirmative. This implies proper timing of the medication so that its period of action is before the bacterial organisms become resistant to Isoniazid.

SUMMARY

1. Twenty-three patients undergoing pulmonary resection for tuberculosis were administered Isoniazid as the prophylactic antibacterial agent during the operative period and postoperatively for a minimum of two months. The efficiency of the drug was measured in terms of postoperative complications due to tuberculosis.

2. The postoperative complications are presented.

3. It is concluded that Isoniazid is a satisfactory prophylactic antibacterial agent for pulmonary resection in tuberculosis.

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DISCUSSION

DR. E. J. O'BRIEN, Detroit.—I am particularly allergic to the pathologic reports we get routinely. You will notice that every one of these slides was labeled fibrocaseous tuberculosis. How much was fibrous and how much was caseous is not answered. This is very, very important.

If there is a lot of fibrous tissue surrounding a small area of caseation, it presents a different problem than a lot of caseation in a small thin capsule of fibrous tissue, and I do hope that our pathologists will be more accurate in their interpretations in the future.

DR. A. C. DANIELS, San Francisco.—A good deal of work on Isoniazid has been done at Weimar Sanatorium and I thought this would be an appropriate time to call to the attention of this group the emergence of strains of tubercle bacilli that are resistant to this drug.

(Slide.) The top line as you will note is Isoniazid alone, and at the end of six months 90 per cent of the strains of tubercle bacilli are resistant to Isoniazid. When it is combined with streptomycin there is essentially the same percentage, 86.9 per cent. With Isoniazid and PAS 80 per cent of the strains of organisms are resistant at the end of six months. When Isoniazid, streptomycin, and PAS are given together, 46 per cent of the strains within six months are resistant to isoniazid. This is a series of about 100 patients, all of whom still had positive sputum at the time the evaluation was carried out, so that we know that these particular strains have developed this resistance.

This is to point out the importance (and I think that is what we learn from Dr. Childress's paper) of preserving Isoniazid as a chemotherapeutic agent for the surgical treatment of tuberculosis and not let it be dissipated at some earlier time when it is not as useful to the patient. So far as we are concerned, the only time that Isoniazid is indicated in the medical treatment of pulmonary tuberculosis is in tuberculous meningitis and miliary tuberculosis, and in those few patients in whom the disease is so far advanced that it is given as a last hope, where no surgical treatment of the patient is anticipated. We hope that the word will get around that Isoniazid should not be used indiscriminately and that it should be reserved for the time of pulmonary resection, because in our hands when used alone it has been a most formidable agent against the tubercle bacillus.

THE INFLUENCE OF LONG-TERM CHEMOTHERAPY ON THE SURGERY OF PULMONARY TUBERCULOSIS

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THE feasibility of the use of long-term streptomycin and PAS in the therapy of pulmonary tuberculosis from the standpoint of toxicity was first pointed out in 1949 by D'Esopo.[1]

Pathologic changes in pulmonary lesions found after prolonged chemotherapy were described about one year later by D'Esopo, Ryan, and Medlar.[2] The surgical excision of necrotic pulmonary foci following long-term original courses of streptomycin and PAS was reported to this Association two years ago by Ryan, Medlar, and Welles.[3] It was suggested at that time that the results from original courses of long-term chemotherapy were more satisfactory than the results from retreatment courses and that the problem of bacillary resistance was not an appreciable one during original courses provided, of course, that combined therapy with streptomycin and PAS was used. It has been shown by the same group of workers that tubercle bacilli can be cultured more readily from the lesions of patients receiving retreatment courses than from those receiving original courses of chemotherapy.[4, 5]

The use of long-term chemotherapy has altered profoundly our own indications for resection and collapse therapy in the treatment of pulmonary tuberculosis. Prolonged chemotherapy is particularly effective in patients having lesions with an appreciable exudative or pneumonic component and is less effective in those having chronic, fibrotic, destructive, irreversible lesions.

In order to appreciate the problems of surgical treatment arising in patients with lesions which show good response to long-term chemotherapy, it is necessary to review certain pathologic concepts. These concepts apply regardless of the extent of the disease.

Medlar[2, 3, 6] has pointed out that as areas of tuberculous pneumonia resolve they may first, either heal by complete resolution or scar formation or, second, undergo necrosis with the formation of an irreversible, necrotic focus which essentially is a tuberculous abscess. The discharge of debris from such a necrotic focus into a bronchus leads to a tuberculous cavity. Chemotherapy apparently hastens the changes which occur in pneumonic lesions. Cavities which are present at the start of long-term chemotherapy frequently become filled with caseous material during treatment and small necrotic areas less than 5 mm. in diameter may sometimes become encapsulated completely. It has recently been observed by Auerbach and his co-workers[7] that the bronchocavitary junction may epithelize as the result of long-term chemotherapy and prevent obliteration of the

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bronchial lumen at this site which, in turn, may be an important factor in preventing cavity closure. Auerbach has further noticed that the inspissated, caseous contents of a filled cavity may be invaded by leukocytes which may produce a liquefaction and evacuation of the contents, leaving a cavity lined with a smooth, glistening surface.

As the result of these observations and of our own observations on resected specimens, we believe that cavities present after long-term original courses of chemotherapy probably fall into three separate categories. In the first group are the filled cavities, the contents of which may vary from hard caseous to liquid purulent material; in the second, there are the "clean" cavities of Auerbach lined with smooth, glistening surfaces which can often be demonstrated roentgenographically to have been filled at some point during chemotherapy; in the third group are the cavities which remain open during the entire course of chemotherapy, and which are usually lined by a "dirty," necrotic, caseous surface. Tubercle bacilli can be cultured much more readily from the walls and contents of these "dirty" cavities than from those in the first two groups (see Table II).[5, 8]

From a practical standpoint, when a patient with disease of relatively recent origin or disease containing an appreciable exudative component is treated with long-term chemotherapy to a point where, first, roentgenograms taken two months apart show no change and all cavities are filled or have been lost to view and, second, examinations of pulmonary secretions are negative on culture, the problem then arises whether to resect the residual lesions or to leave them alone. We have chosen to use resection for such patients except for those who have extremely small exudative lesions prior to chemotherapy.

We realize that final evaluation of our resection program will require a fairly long follow-up period. The incidence of reactivation of disease in the resection group must be compared with that in a comparable group which has received long-term chemotherapy without resection.

We do not believe that collapse therapy can be considered logically as an alternative in these cases because of the nature of the pathology of the residual lesions.

We do, however, believe there still is a place for collapse therapy, particularly thoracoplasty, in the treatment of tuberculosis. The relative frequency with which collapse therapy procedures were used in relation to resection at our sanatorium during 1952 is shown in Table I.

TABLE I. SURGICAL AND COLLAPSE THERAPY PROCEDURES USED DURING 1952 AT MUIRDALE SANATORIUM

PROCEDURE	PATIENTS
Resection	128
Thoracoplasty (definitive)	17
Decortication	3
Paraffin pneumonolysis	1
Phrenic paralysis	1
Pneumoperitoneum	1
Pneumothorax	0

In general we have used thoracoplasty in patients with cavities remaining open during long-term chemotherapy and who have also had disease which appeared too extensive for resection. In addition, we have been inclined to use thoracoplasty when the operative risk of resection was estimated to be abnormally high. We do not consider that we have abandoned other collapse therapy procedures entirely and intend to use them in occasional selected cases in the future. We feel that long-term chemotherapy is so much more effective than the so-called temporary collapse therapy procedures that we are fully justified in not using them to any appreciable extent.

Our present program of resection of residual necrotic foci following long-term chemotherapy started in June, 1951, when we operated on a patient who had received an original course of streptomycin and PAS of sixteen months' duration. From June, 1951, to December, 1952, we performed 182 pulmonary resections on 146 patients. One hundred twenty-five of these resections were for residual lesions in patients prepared with original courses of streptomycin and PAS for four months or more; twenty-one patients were prepared with long-term retreatment courses; the preparation or indication for thirty-six other patients who underwent resections for pulmonary tuberculosis performed during this same period are shown in Table II.

TABLE II. MISCELLANEOUS RESECTIONS FOR TUBERCULOSIS IN 34 PATIENTS

	RESECTIONS	CULTURE POSITIVE
Cavities unfilled during chemotherapy	10	7
Less than 4 mo. chemotherapy preparation	13	2
Isoniazid preparation 1-4 mo.	4	1
8 mo.	5	1
Other	4	0
Total	36	11

The type of operations performed on our patients who received long-term chemotherapy in preparation for resection is shown in Table III. The great majority had small resections, either wedges or segments or both. Wedge resections were performed during 93 of the 146 operations. These wedge resections were actually subsegmental resections since all dissections were carried out in anatomic planes. The pneumonectomy was performed because the pulmonary artery was torn during a segmental resection.

We believe that the use of long-term chemotherapy made it possible to perform small resections in the majority of our patients and thus preserve con-

TABLE III. TYPE OF PULMONARY RESECTIONS IN 112 PATIENTS WITH FOUR OR MORE MONTHS' PREOPERATIVE SM AND PAS
(ORIGINAL AND RETREATMENT COURSES)

Exploration only	4
Wedge(s) only	63
Segment(s) only	39
Segment(s) plus wedge(s)	27
Lobectomy only	9
Lobectomy plus wedge(s)	3
Pneumonectomy	1
Total	146

siderable pulmonary function. In other words, the percentage of entire lobes resected would have been much higher if these patients had been prepared for resection with short courses of chemotherapy.

Pulmonary function, as measured by maximum breathing capacity and walking ventilation, was not affected in the great majority of our patients having small resections, even in the bilateral cases.

The greatest disadvantage we have found in the performance of small resections has been the relatively high incidence of postoperative complications. These complications and the treatment required in each group are listed in Table IV. We should like to emphasize: (1) that the end results in all of these patients have been good, (2) that none of the complications was tuberculous, and (3) that there was no mortality in this group of 146 resections. We feel that the high incidence of peripheral lung leaks, as distinguished from large bronchial leaks, is a reasonable price which has been paid for the preservation of a maximum amount of lung tissue. The lung leaks considered as complications were either persistent or recurrent. We believe that it is usually safer to perform a secondary thoracotomy than to rely on the use of catheters and needles over a protracted postoperative period. This is particularly true in the case of postoperative hemothorax. It is possible that two empyemas could have been prevented if hemothoraces in these patients had been evacuated early by secondary thoracotomy. Our space-filling thoracoplasties were small ones and resulted in no appreciable loss of pulmonary function.

TABLE IV. SIGNIFICANT COMPLICATIONS AND TREATMENT REQUIRED
146 RESECTIONS—112 PATIENTS

I. Lung leaks		19
Secondary thoracotomy	13	
Catheter aspiration	5	
Space-filling thoracoplasty	4	
II. Hemothorax		6
Secondary thoracotomy	3	
"Varidase" (successful)	1	
Space-filling thoracoplasty	2	
III. Empyema (pyogenic)		5
Thoracotomy for drainage	5	
Modified thoracoplasty	5	
Total complications		30 (20.0%)

Table V shows the distribution of the complications according to the types of small resections. Although a number of different operative techniques and postoperative routines were utilized, the incidence of complications was evenly distributed throughout the series.

TABLE V. SIGNIFICANT COMPLICATIONS IN 129 SMALL RESECTIONS

	CASES	PER CENT	NO.
Wedge(s) only	63	9	14
Segment(s) only	39	8	20
Segment(s) plus wedge(s)	27	11	40

We have been particularly interested in the bacteriology of the resected lesions from patients who have received long-term chemotherapy. For the most part, the material from different lesions in the same resected specimen was pooled for bacteriologic examination. Lesions were incised for examination by the surgeon under aseptic conditions at the conclusion of each operation. Cultures and guinea pig inoculations were done on untreated material and also on another portion digested with trisodium phosphate. Cultures were made on Löwenstein-Jensen's medium. Guinea pig pathogenicity and drug sensitivity tests were made on all positive cultures.

Fortunately, the number of our patients receiving long-term *retreatment* courses of streptomycin and PAS was relatively small. The reason for this is that we had complete control of the choice and administration of the chemotherapy received by most of our patients. Furthermore, we were aware two years ago of the probable advantages of original over retreatment courses. Five of the twenty-one resected specimens in this group were positive on culture (Table VI). This incidence corresponds closely to the findings of others in this category.[4, 5, 8] All of our patients had drug-sensitive bacilli at the time of retreatment.

TABLE VI. BACTERIOLOGY OF RESECTED LESIONS IN 16 PATIENTS HAVING RETREATMENT COURSES OF SM AND PAS FOR MORE THAN FOUR MONTHS TOTAL THERAPY—VARIOUS REGIMENS

MONTHS CHEMOTHERAPY	RESECTIONS	CULTURE AND/OR GUINEA PIG POSITIVE
4- 8	5	1
8-12	9	3
12-18	5	1
18-24	2	0
Total	21	5

In the group of patients who had *original* courses of streptomycin and PAS for more than four months (Table VII), 125 resections were performed on 96 patients. In other words, twenty-nine patients had bilateral and sixty-seven had unilateral resections. One hundred two patients were prepared with eight or more months of chemotherapy.

TABLE VII. BACTERIOLOGY OF RESECTED LESIONS IN 96 PATIENTS HAVING ORIGINAL COURSES OF SM AND PAS FOR MORE THAN FOUR MONTHS

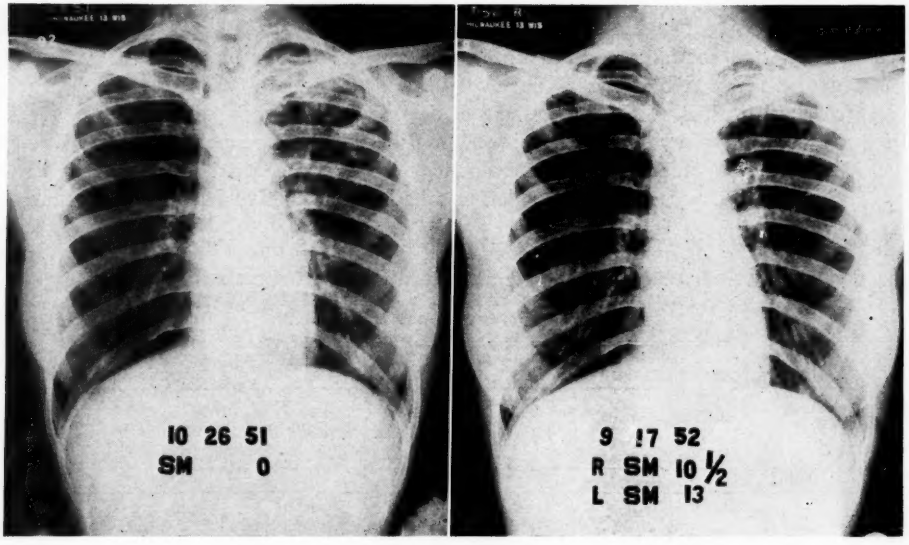
MONTHS CHEMOTHERAPY	RESECTIONS	SMEAR AND/OR SECTION POSITIVE	CULTURE AND/OR GUINEA PIG POSITIVE	NONCASEOUS LESIONS OR NONE
4- 8	23	14	1	5
8-12	54	37	3	3
12-18	46	26	7	4
18-24	2	2	0	0
Total	125	79	11	12

Cultures of the sputum or gastric contents of eighty-eight of these patients were positive for tubercle bacilli prior to the start of chemotherapy; the lesions of the other eight patients were active from a roentgenographic standpoint.

The pulmonary secretions of only one of the ninety-six patients were known to be positive on culture just prior to resection; the secretions of eighty-six patients were negative; the secretions of nine patients early in our series were not examined immediately before resection.

Roentgenologic stability of lesions for a minimum of two months was required prior to thoracotomy.

The lesions in 105 of the 125 lungs showed moderate to marked roentgenologic improvement under chemotherapy while the lesions in the other 20 remained stationary.



A. *B.*

Fig. 1 (Case 1).—The patient was a white woman, 26 years old. *A*, Roentgenogram at start of chemotherapy. Note large subclavicular cavity on left. *B*, Roentgenogram following ten and one-half months of chemotherapy consisting of daily doses of streptomycin and PAS. Preoperative film. For operative findings see Fig. 2, *A* and *B*.

Four patients having cavities lined with smooth, glistening surfaces which had shown roentgenographic evidence of having been filled at some point during chemotherapy are included in this group of 96 patients. No patient having a cavity which had not closed or which had not been filled during chemotherapy is included.

The discrepancy between the number of positive smears and/or acid-fast bacilli found on tissue section and the number of positive cultures or guinea pigs brings up the question as to whether such tubercle bacilli which can be seen but cannot be grown are dead or alive. Some investigators[9, 10] believe that such bacilli in most lesions are actually dead. On the other hand, it has been suggested that these bacilli may have lost their ability to reproduce because they may be affected by a substance or substances which, if neutralized, might allow them to reproduce again.[11] This is a question which cannot be answered at the present time.

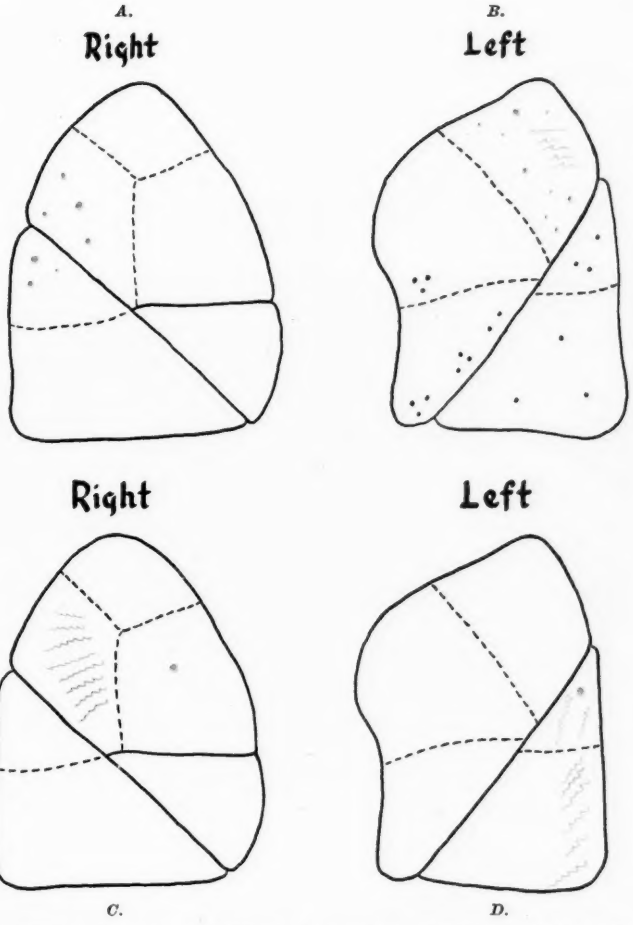
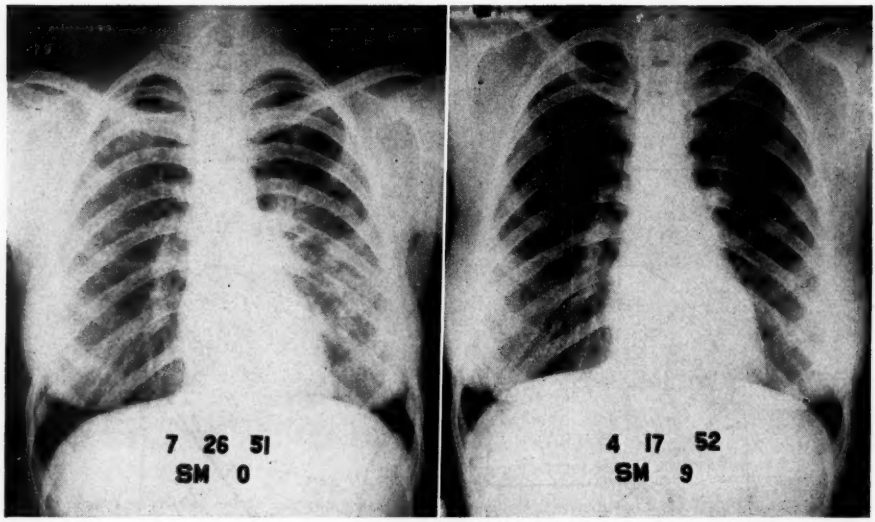


Fig. 2 (Cases 1 and 2).—*A*, Diagram of operative findings on right in Case 1. The posterior segment and a wedge from the superior segment were resected. The resected nodular lesions (shown in red) measured up to 1 cm. in diameter. Some lesions contained soft, and others hard, caseous material. *B*, Operative findings on left in Case 1. The apical-posterior segment was resected. The resected nodules (shown in red) contained hard to semiliquid caseous material. Culture of this material was positive on culture for tubercle bacilli. The wavy lines indicate fibrosis. None of the unresected nodules (shown in black) was over 2 mm. in diameter. *C*, Operative findings on right in Case 2. The posterior segment and wedge from the anterior segment were resected. Material from the 5 mm. nodule in the anterior segment was positive on smear and culture. *D*, Operative findings on the left in Case 2. Two wedges were resected. Material from the 5 mm. nodule was positive on smear but negative on culture.

We do know, however, that the tubercle bacilli recovered from the lesions of some of our patients did grow and did produce disease in guinea pigs. The eleven resected specimens which yielded tubercle bacilli which grew on culture or produced disease in a guinea pig were from eleven different patients; none of these patients had positive cultures or guinea pig inoculations of resected lesions from both lungs. These patients had original preoperative courses of chemotherapy varying in length from six to fifteen months.

The twelve operations in the last column (of Table VII) emphasize the difficulty in using roentgenographic findings as an indication of the presence or character of residual lesions (see Figs. 4 and 5). Four of the twelve operations were actually exploratory thoracotomies rather than resections as no palpable disease was found; the resected specimens from the other eight lungs

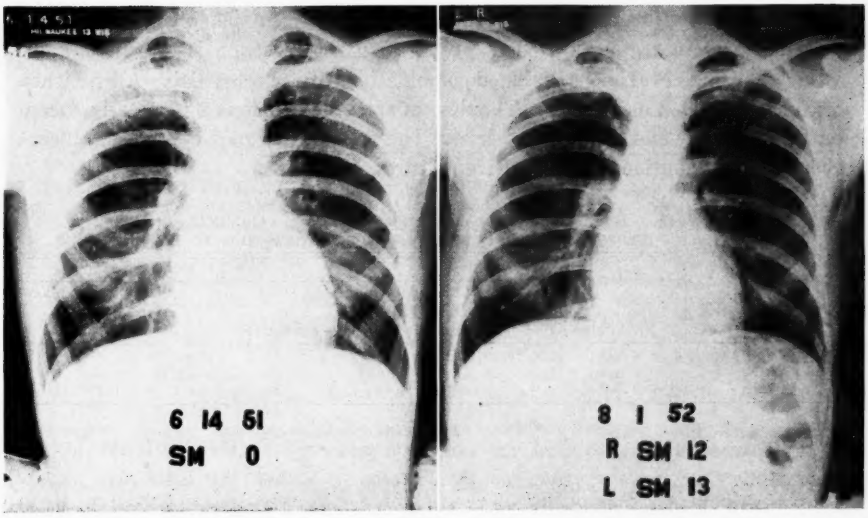


A. *B.*

Fig. 3 (Case 2).—The patient was a 26-year-old white woman. *A*, Roentgenogram at start of chemotherapy. *B*, Roentgenogram after nine months of chemotherapy. Preoperative film. For operative findings see Fig. 2, *C* and *D*.

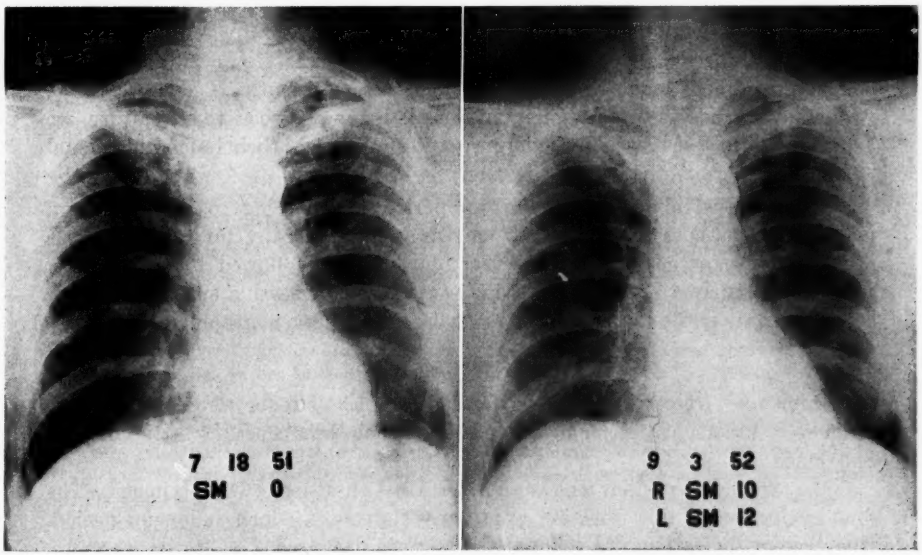
contained fibrous tissue only although in two of these, acid-fast bacilli were demonstrated in microscopic tissue sections. Ten patients are represented in these twelve "dry runs," two having had "dry runs" on both sides. Nine of these ten patients had had positive cultures of sputum or gastric contents just prior to chemotherapy; all lesions had shown definite roentgenologic improvement on chemotherapy. On reviewing the indications for thoracotomy in these twelve cases, we found only one which, in retrospect, we would not have explored again.

All palpable disease was resected from 91 of the 125 lungs and, as noted, four patients had no palpable disease. So much disease was present in 3 of the 125 lungs that resections were performed as biopsies only, to determine the character and bacteriology of a few of the lesions present.



A. *B.*

Fig. 4 (Case 3).—The patient was a 46-year-old white woman. *A*, Roentgenogram at start of chemotherapy. *B*, Roentgenogram following twelve months of chemotherapy (preoperative film). Lesions resected on right contained fibrosis only with the exception on one 3 mm. caseous nodule. Lesions resected from left lung contained diffuse fibrosis only.



A. *B.*

Fig. 5 (Case 4).—The patient was a 52-year-old white man. *A*, Roentgenogram at start of chemotherapy. *B*, Roentgenogram following ten months of chemotherapy (preoperative film). Lesions resected from right lung contained fibrosis only. Lesions from left lung contained one 3 mm. caseous nodule in addition to considerable fibrosis.

The distribution of our positive cultures and/or guinea pigs according to the streptomycin regimens used in preparation for resection is shown in Table VIII. The mixed regimens included combinations of the other two. All patients, of course, received daily PAS. The dose of streptomycin was 1 Gm. daily except in the case of the one child in the series. There is nothing particularly significant about the distribution of the positive cultures.

TABLE VIII. BACTERIOLOGY OF RESECTED LESIONS. ORIGINAL COURSES. DISTRIBUTION OF RESECTIONS AND POSITIVE CULTURES ACCORDING TO SM REGIMENS

	4-8 MONTHS		8-24 MONTHS	
SM REGIMEN	RESECTIONS	CULTURE AND/OR GUINEA PIG POSITIVE	RESECTIONS	CULTURE AND/OR GUINEA PIG POSITIVE
Daily	16	1	33	3
2x week	6	0	39	3
Mixed	1	0	30	4

We were unable to find anything particularly characteristic about the pretreatment or preoperative roentgenograms of either the cases which subsequently yielded positive cultures (or guinea pigs) of their lesions or the cases which had no palpable disease or predominately fibrotic disease. The roentgenograms and operative findings of two representative cases from the former group are illustrated in Figs. 1 to 3; the roentgenograms of two patients from the latter group will be found in Figs. 4 and 5.

In all of our patients whose lesions were resected following preparation with long-term chemotherapy we have continued chemotherapy for an arbitrary postoperative period of three months. Patients having significant unresected disease have had longer postoperative courses. Recently, because of late recurrence of disease in two patients whose lesions were positive on culture, we have decided to give patients who have positive cultures of their lesions additional postoperative chemotherapy.

As indicated above, our follow-up period is too short to be significant. Only thirty patients prepared with long-term chemotherapy for resection have been followed for one year. However, four patients followed for less than a year have recurrent disease. Two of these have had positive cultures of their secretions only while the other two have also had roentgenographic recurrences.

SUMMARY

Pulmonary resections were performed on 112 patients whose tuberculous pulmonary lesions had responded favorably to long-term courses of streptomycin and PAS.

Bacteriologic examinations were carried out on all resected specimens. The final evaluation of this resection program will require a long follow-up period. Our present indications for collapse therapy are discussed.

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DISCUSSION

COLONEL JAMES H. FORSEE, Denver.—It may be of interest to report briefly certain follow-up data regarding patients treated at Fitzsimons Hospital during the period from January, 1947, to approximately one year ago.

Three hundred sixty-nine patients received extirpative surgery. An interesting fact is that the disease process in this group of patients, preoperatively in 60 per cent, whether cavitary or noncavitary, was limited to an area involving only one lobe and limited in extent to an area no greater than that above the level of the second costochondral junction. This is the classification of minimal tuberculosis, but these patients are not minimal tuberculosis; 30 per cent had cavitary lesions.

The surgical procedures employed in this 60 per cent, or 221 patients, was lobectomy in 52 per cent, wedge resection in 31 per cent, and segmental resection in 17 per cent. The follow-up data approximately one year to more than five years as available in 97.3 per cent. Of these patients 93 per cent are living and well; three patients, or slightly over 1 per cent, are dead (none due to tuberculosis); five patients, or 2.3 per cent, had reactivation of the disease occurring at intervals of four to eleven months postoperatively. The reactivation of previously unrecognized foci occurred on the side of the resection in three patients, and on the contralateral side in one patient. Bacteriologic relapse occurred in one instance without evidence of reactivation or new pulmonary lesions. In three of these five, the patient had cavitary disease. Glandular tuberculosis occurred in two patients or .9 per cent; one occurred four years after pulmonary resection. The other was a reactivation of previously existing cervical adenitis four years after operation. At this time 57 per cent of these patients are gainfully employed, part or full time; 36 per cent are well but have not returned to work. Seventy-one of the 221 patients have been operated on since 1951.

To us, these facts reveal that more and more patients with less and less pulmonary tuberculosis are being successfully treated by surgery. It seems reaonable to anticipate that this is the trend in the surgical management of pulmonary tuberculosis since the advent of the antituberculosis drugs. And it seems reasonable to predict that, if the disease is detected early, if proper therapy is instituted and carried to its completion, more than 90 per cent of

patients with uncomplicated pulmonary tuberculosis will recover and return to active gainful occupation—a great tribute to many of those in this audience today who have devoted so much of their lives to the treatment of pulmonary tuberculosis.

DR. E. J. O'BRIEN, Detroit.—I have been very much interested in Dr. Steele's paper, but it was very difficult for me to follow him. He spoke constantly of long-term treatment, and yet slide after slide went on the screen where the long-term treatment was shown as from four to eight months. That is not long-term treatment. He also questions the value of thoracoplasty after long-term treatment, though the cavities are still open. Many of the rest of us believe that cavities not closed after six months will not close under this regimen alone, and that thoracoplasty or some other collapse measure should be used to assist in closure, unless resection seems indicated.

He mentions producing disease in guinea pigs from cultures or caseous material after so-called long-term treatment. I believe I have read about all the literature that has been published on the subject, and I have yet to find a report from anybody who has produced disease in guinea pigs after what is really continuous long-term treatment. I looked over Dr. Steele's figures yesterday and he has not produced disease in quinea pigs after sixteen months of chemotherapy had been given.

DR. STEELE (Closing).—The matter of what should be called long-term therapy is very arbitrary. We arbitrarily selected four months as a minimum for our long-term cases. However, I would like to remind you that we had 102 resections on patients receiving original courses of streptomycin and PAS of eight months or more, and that the viable, pathogenic bacilli which we recovered were from eleven patients receiving from six to fifteen months of original courses of long-term chemotherapy.

SEGMENTAL RESECTION FOR PULMONARY TUBERCULOSIS (300 CASES)

J. MAXWELL CHAMBERLAIN, M.D., CAPTAIN CLIFFORD F. STOREY, MEDICAL CORPS, UNITED STATES NAVY, ROBERT KLOPSTOCK, M.D., AND CHARLES F. DANIELS, M.D. (BY INVITATION)
NEW YORK, N. Y.

INTRODUCTION

SEGMENTAL resection in the surgical management of pulmonary tuberculosis is now an established and accepted procedure.[1-28] It can be used in minimal, moderate, and far-advanced cases of pulmonary tuberculosis provided the major offending focus is limited to one or two segments of the lobe. The rate of sputum conversion is high and with experience the morbidity and mortality rates are low. The operation is moderately intricate and demands great postoperative vigilance, but it avoids prolonged hospitalization and, by corollary, reduces the task of rehabilitation. Its greatest virtue, of course, is its preservation of pulmonary function as was intended by its originator, Dr. E. D. Churchill,[29] and other early workers.[30-33]

BASIC PATHOLOGY

Tuberculosis usually begins as a "patch" of indolent pneumonia confined to the upper and posterior segments of the lobes as reported by Medlar and others.[34-36] Less frequently it may involve a lobe or the entire lung but regardless of its dimensions it begins as a pneumonia.

The patch of pneumonia may take three courses: (1) resolution, (2) fibrosis, or (3) caseation necrosis. If resolution of the exudative element occurs, the alveolar walls remain intact, no function is lost, and ultimately all evidence of the disease disappears from the chest film. If fibrosis occurs the area is replaced by "scar" tissue (the productive reaction), alveolar function is lost, and the x-ray film always reveals the site of the insult. In other instances small "patches" of pneumonia coalesce to form a large conglomerate area. If the vascular nutrition to the center of this area is lost, caseation necrosis occurs and the alveolar architecture is destroyed. Usually one or more small bronchi communicate with the necrotic area, and should liquefaction of this caseous material occur the area "shells out" to form a cavity.

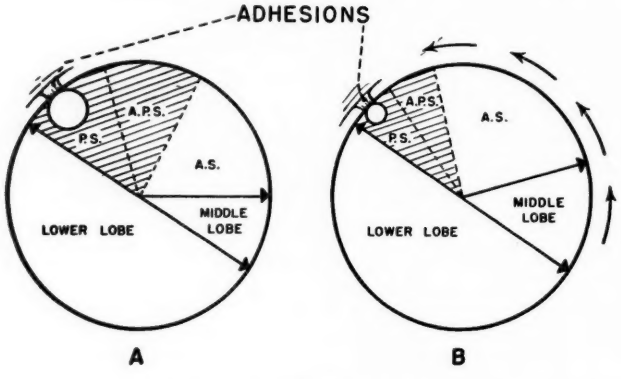
In every lesion probably all three factors are at work. There is some resolution, some fibrosis, and some caseation necrosis. It is the necrotic focus, and especially the size of this focus, that threatens the patient's future welfare. Through liquefaction of this necrotic area bronchial dissemination of the disease may occur. Segmental or subsegmental resection performed at the proper time is designed to avoid such spreads.

The opinions or assertions expressed in this paper are private ones of the authors and are not to be construed to be official or to reflect the views of the Navy Department or the Naval Service at large.

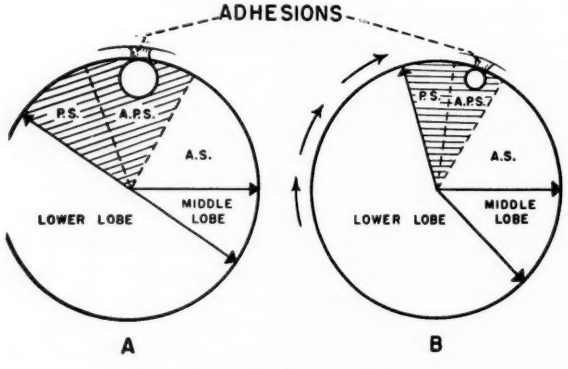
Read at the Thirty-third Annual Meeting of The American Association for Thoracic Surgery, San Francisco, Calif., March 27, 28, and 30, 1953.

BASIC PHYSIOPATHOLOGY

The functional advantages of leaving behind only one of three segments of a lobe was at first debatable. It was reasoned, however, that as a functional unit it contributed its bit to the total function and as a "filler" it prevented excessive distention of the residual lung components and in this way preserved their function. We now know by actual bronchospirometric measurement performed on a series of these patients before and after segmental resection that little or no function is lost and in some cases it seems to be actually improved. One of us (C. F. S.) will report on this functional aspect at a later date.



SEGMENTAL CLOCK
(RIGHT LATERAL VIEW)



SEGMENTAL CLOCK
(RIGHT LATERAL VIEW)

Fig. 1.

The residual segments are usually larger than normal, and the presence of adhesions may determine which segments will enlarge to compensate for the healing and contraction in the diseased segments. For example, ad-

hesions between the right posterior segment and the chest wall will not permit enlargement and upward movement of the lower lobe as healing and contraction occur in the apical and posterior segments. However, with the hilum of the lung as an axis, a counterclockwise enlargement of the anterior segment and the middle lobe is often observed (Fig. 1). On the other hand, if adhesions exist between the right apical segment and the thoracic vault as healing and contraction occur the lower lobe enlarges and rises high in the pleural cavity. In such cases there is less demand for the anterior segment and middle lobe to enlarge. The segments in which the enlargement is greatest are in cases free of adhesions. Conversely, an obliterative pleuritis seems to prevent not only the contraction of the diseased segments, but any significant enlargement of the healthy components as well.

INDICATIONS

The main indication for segmental resection is the necrotic lesion. Necrotic lesions may be small, medium, or large and still confined to one or two segments of a lobe. Not only is the size of the necrotic focus important, but also its duration and especially the amount of associated exudative or pneumonic disease.

The duration of the lesion is significant because it is difficult in the chest film to distinguish the boundaries between shadows due to exudative, fibrotic, or necrotic disease. It may be reasoned, though not without an element of doubt, that if the lesion has been present in serial x-ray films for some time, it is predominantly a fibrocaseous lesion. In other words, the acute exudative or pneumonic elements have probably resolved. If, however, the shadow is being viewed for the first time this assumption may be inaccurate.

The size of the necrotic focus is important because the small foci are drained in most instances by small bronchi and the large ones are drained by large bronchi. It seems reasonable to suppose that the caseous material undergoing liquefaction will drain more easily through a large bronchus than through a small one, and perhaps it follows that it "spreads" more easily as well. These points require further proof.

Exudative disease can be expected to respond to conservative management and antibiotic therapy permitting the dimensions of the operative procedure to be reduced. Emergency operations have been successfully performed in the presence of acute tuberculous pneumonia, because of hemorrhage, cavity rupture, and extensive pneumonic "spreads,"[37] but in general, major thoracic procedures, including thoracoplasty, should not be done in the presence of significant exudative or pneumonic disease.

The ideal indication for segmental resection is the fibrocaseous lesion with or without a cavity and devoid of an exudative element. The focus should be of such size and duration that mature medical opinion is doubtful of the patient's future security.

PREOPERATIVE STUDY AND PREPARATION

Laminography, especially the lateral sections, introduced by one of us (R. K.),[3] gives an extremely valuable preview to the thoracotomy. The phrase

"bloodless thoracotomy" applied to laminography seems justifiable to those accustomed to its use. Perhaps no other preoperative study is more helpful to the surgeon.[2, 38, 39] The exact location of the disease, and especially the appearance of the segments to be left behind, may be learned from these studies. As experience in the use of laminography increases, it is rare for the surgeon to perform a lobectomy when a segmental resection was intended. If a segmental resection is contemplated, a rib is usually not removed, the chest being entered through an intercostal incision since a tailoring surgical procedure after a segmental resection is usually unnecessary.

The specific antibiotics are given for variable lengths of time prior to the operation, but always until the exudative element surrounding the fibrocaseous focus is thought to be absent. Other preoperative studies are similar to those which should precede any major surgical operation.

TECHNIQUE—OPERATION

Prior to operation as a result of lateral laminography the surgeon is reasonably aware of the pathology and its dimensions. The segments to be removed have been decided upon and the bronchi to these segments are immediately isolated and clamped before unnecessary manipulation or mobilization of the lung. (There are anatomic exceptions to this plan.) Gentle palpation of the pathologic lesion usually confirms the decision reached through the use of laminography. After the segmental bronchi have been clamped and divided, the lobe is then mobilized with impunity since secretions can no longer be expressed into the bronchial tree. Occasionally after palpation our interpretation of the laminographs proves inaccurate and it is necessary to remove an additional segment or subsegment.

The arteries to the segment are then isolated, ligated, and divided. Preservation of the intersegmental veins is desirable when only one segment is removed, but when two segments are removed it is necessary to remove the intersegmental vein with the specimen. The intersegmental plane is then developed by gentle traction and dissection as described by Clagett.[32] Bleeding from the raw area is meticulously controlled. No effort is made to cover the raw area with pleura as was previously described[6]; any attempt to close it will only distort the segment and interfere with its ability to "breathe." Furthermore, were the raw area to be closed, in all probability the sutures would cut out in the next few days during deep breathing or coughing. The bronchus is then reamputated and closed with interrupted silk sutures. Pleuralization of the bronchial stump is not always done. Usually the residual segment or adjacent lobe seals the bronchus upon complete re-expansion. Two tubes are left in for drainage and re-expansion. One tube is anterolateral and fixed with a suture to the pleura of the thoracic vault. The other tube is low and in a posterolateral position. The wound is closed in anatomic layers and a small narrow dressing is applied in order to allow adequate clinical examination of the chest during the immediate postoperative period. The large firm

dressing physiologically simulates the so-called captive lung mechanism. Unilateral tidal loss is significant.[40] The two tubes are connected to a "Y" tube and placed upon active suction (see Discussion).

POSTOPERATIVE REGIME

At the completion of the hilar dissection the residual segments are inflated, the intercostal tubes are placed, and intrapleural suction is established simultaneously with wound closure. Approximately 200 c.c. of saline solution are left in the pleural cavity to dilute the small amount of blood which gravitates to the dependent parts of the hemithorax during wound closure. The dilution of blood by the saline solution prevents clot formation and helps to insure patency of the tubes during the early postoperative period. Most of the saline solution is immediately removed by the suction system as wound closure is completed. A compact portable suction pump is used to maintain the desired intrapleural pressure during transportation from the operating room. This maneuver, though not essential, is an additional precaution to insure immediate and complete re-expansion of the residual lung components.

The patient's position in bed is at first on the side of the operation. Later he is turned to his back and for effective coughing he is allowed to assume the sitting position. Young people with muscular diaphragms will tolerate slight elevation of the foot of the bed. This allows the fluid to gravitate to the thoracic vault and keeps the costophrenic angle sharp. The fluid is then removed through the upper tube and the pleural reaction is confined mainly to the thoracic vault. "Pleurisy" which binds or fixes the diaphragm may significantly influence function. Pleural reaction in the thoracic vault is of little functional significance.

Intrapleural suction is usually set at a minus 15 to 25 cm. of water. Pressures at a minus 5 to 10 cm. of water are basal-physiologic. Intrapleural suction is usually set at a minus 15 to 25 cm. of water, pressures at a minus 5 to 10 cm. of water are basal-physiologic. End-operative studies on the bronchospirometric contribution of the individual lung have revealed that pleural suction in the range minus 5 to minus 16 in fact results in a control subtidal, ipsilateral ventilation. Maximum tidal volume occurs with negative pressures in the range of minus 18 to minus 20. It should be noted that Lindskog found experimentally that reinflation via collateral ventilation requires a gradient of some 16 cm. of water.

If the segments are to remain inflated the bronchi and bronchioles must not become occluded by blood or secretions. Clots of blood in the small bronchioles may be propagated to larger and larger divisions to produce a segmental atelectasis. On the other hand, if good air flow is maintained up through the bronchioles and out through the small alveolar leaks, secretions do not collect to account for subsegmental or segmental atelectasis. In our experience active suction does not prolong alveolar leaking. In the majority of cases the tubes can be removed in forty-eight to seventy-two hours, but tubes are never removed at night. It seems preferable to remove them in the morning when a full complement of nurses and doctors is available, should a pneumothorax develop. A roentgenogram is taken a few hours after the

tubes have been removed with a portable chest x-ray machine to determine the degree of lung expansion. A sterile trocar, cannula, and catheter are always available and suction is re-established immediately should a "late leak" develop. Complete and early re-expansion seems essential in the prevention of an empyema or bronchopleural fistula.

Patent airways, large and small, are essential to successful re-expansion. Ciliary action, bronchial peristalsis (elongation and foreshortening of bronchus during the respiratory cycle), and cough are the patient's protection against spreads and atelectasis. The patient is urged by the nurse to take thirty deep breaths every half hour during his waking hours. Furthermore, he is encouraged to help turn himself in bed frequently. This exercise promotes deep breathing. However, intratracheal suction each morning and night during the first forty-eight hours is perhaps the most important postoperative assistance the patient can be given. Its disagreeable aspects, if nothing else, assures patient cooperation throughout the day whenever he is urged to cough by the nurse in attendance.

Pain is caused by the incision, muscle spasm, the divided ribs, and the pleura. Little can be done about the incisional pain. The muscle spasm can be reduced by frequent passive and active shoulder girdle exercises. Fixation of the divided ribs during closure will prevent pain arising from the fracture site, but pain from the pleura is more difficult to control. The parietal pleura is very sensitive and the visceral surface of the residual segments is altered: (1) by operative manipulation (gauze abdominal pads, sponges, etc.); and (2) by the precipitation of fibrin as a result of the mild but ever present hemothorax. The movements of these residual lung components against the parietal pleura, plus the pleural irritation of the drainage tubes, are probably responsible for most of the pain. This theory is supported further by the fact that patients after a pneumonectomy have much less pain than patients after a lobectomy or a segmental resection.

Since patent airways are essential to re-expansion and perhaps life, and since coughing and deep breathing are painful, it follows that the control of pain is extremely important. Narcotics, not sedatives, will control pain. Their frequent use in moderate dosage is encouraged. The use of narcotics in chest disease earned its bad reputation in the primordial stages of our learning. Vigilant nursing and a regimented postoperative plan will not allow the patient to slip into narcotic coma and drown in his own secretions.

Specific antibiotics are used routinely after operation. They are continued for various lengths of time as determined by the attending physician, usually for not less than three months. The nonspecific antibiotics are used one day before surgery, at operation, and for the first week after surgery. Nontuberculous empyema and wound infections have played no significant role in this series.

Transfusions are used during and after operations to maintain blood volume. Usually 1,500 to 2,000 c.c. of blood is given each patient.

Ambulation is permitted during the first two weeks after operation to encourage costal and diaphragmatic breathing. Early restricted activity may

lead to high fixation of the diaphragm and cause a corresponding decrease in respiratory function. The patient returns to bed after two weeks and remains there usually for three months except for lavatory privileges. Activity is then increased again.

The use of oxygen in segmental resection is important in the older patient, but it is rarely necessary in the young patient with good coronary circulation. The temporary costal and diaphragmatic restriction after operation creates a "shunt" and the oxygen saturation of the blood does not return to normal for a variable number of days. In the older patients the coronary circulation is an unknown factor. In this group the generous and prolonged use of nasal oxygen is encouraged. Nasal oxygen seems preferable since these patients require a great deal of nursing attention which is difficult to administer if a tent is used.

"Diet as tolerated" is not that simple. Abdominal distention with elevation of the diaphragm is a frequent postoperative complication which may embarrass respiration. Clear liquids are given the first day supplemented by intravenous fluids if necessary. On the second day nourishing liquids, soups, custards, etc., are usually tolerated. However, an unexplained elevation in pulse rate in a patient who is not vomiting may be an indication for gastric decompression. In muscular young men gastric distention is not as obvious as in atonic women or older men. Acute gastric distention, therefore, should be suspected in every muscular young man whose fluid intake is adequate, but who remains thirsty, runs a rapid unexplained pulse, and is not vomiting.

An upright posteroanterior and lateral x-ray film is taken on the first postoperative day with a portable machine. A second is taken on the day the tubes are removed (usually the second or third postoperative day). A third is taken on the fourth or fifth postoperative day. After that the patient is well enough to stand for fluoroscopy at frequent and regular intervals. Such vigilance is necessary since "late leaks" seem to occur in about 5 to 10 per cent of the patients, and immediate intercostal intubation will avoid the complications associated with the unexpanded lung. On several occasions we have had to intubate a patient more than twice. A late leak developed in one patient on the fourteenth postoperative day, one day before discharge. In another patient it did not develop until the forty-first postoperative day. The "late leak" is considered a minor complication because these patients need not return to the operating room for intubation and it is extremely rare for the "late leak" to progress and cause a major complication, such as empyema or bronchial fistula.

DISCUSSION

Pulmonary tuberculosis is usually bilateral though not necessarily bilaterally active. The advocates of segmental resection are the first to admit that only the major offending focus or foci are removed by this procedure. Foci are almost always present in the opposite lung or in the residual lung components on the side of the operation. These foci are also present in patients successfully treated by other forms of therapy such as bed rest, pneumothorax,

or thoracoplasty. Removal of *all* of them is technically impossible and probably unnecessary. The decision to remove other foci is dependent upon size and location.

The actual size of the hazardous lesion is difficult to estimate in centimeters. Usually a large lesion is more hazardous than a small one, but on the other hand a small lesion in a patient without resistance can be more hazardous than a much larger one in a patient who seems "unable to handle his disease." Furthermore, it is noted by those in the field of experimental research, by the pathologist and by the clinician, that lesions in the anterior and dependent segments of a lobe are less hazardous than those in the posterior and apical segments. Cavities located anteriorly are recalled only because they are exceptions to the rule or because they began in the apical-posterior segments and extended into the anterior and dependent areas. A lesion requiring resection in the superior segment[6] of the lower lobe may safely remain in the tip of the lingula. To molest the various lobes by attempting to remove locally all foci, large and small, without regard for location ignores this basic information and subjects the patient to unnecessary morbidity and perhaps mortality. This belief is based not only upon our recent and short experience with segmental resection, but upon a comparatively long experience with the thoracoplasty procedure. Though the therapy has changed the location of tuberculosis is the same. Therefore, there must have been foci anteriorly in the days when the thoracoplasty was our most popular form of surgical therapy. Yet our failures were not usually due to the "breakdown" of lesions anteriorly where the collapse was least, but due to unclosed cavities posteriorly where the collapse was greatest. It is not implied, however, that tuberculosis located anteriorly should not be respected.

Overdistention of the residual segments after segmental resection is less than after lobectomy and pneumonectomy. Physiologically, respiratory function is inversely proportional to the degree of emphysema caused by overdistention. Lung elasticity is variable,[40] and in all patients with tuberculosis there exists a variable amount of emphysema. Laennec, without a microscope, described focal emphysema surrounding every healed and contracted lesion. The physiologic effects of overdistention are much more noticeable in the older patient with horizontal ribs and a thick anteroposterior diameter than in the slender young patient with oblique ribs and a comparatively narrow chest. There must be a limit to the amount of distention a lung can tolerate before actual alveolar wall destruction occurs. The speed and duration of overdistention are also factors. Tuberculosis is an indolent disease which heals slowly. As healing and contraction of the diseased segments occur, a slow compensatory enlargement of the healthy parenchyma takes place. The undesirable aspects of suddenly demanding a single lobe to fill one chest after a lobectomy has led us to believe that a small tailoring procedure should be done simultaneously.

Overdistention may or may not be responsible for the "breakdown" or reactivation of disease in the residual segments. A point less debatable is the fact that should a breakdown occur the emphysematous patient does poorly

with tuberculosis and usually to an extent inversely proportional to the amount of emphysema. It is thought that one of the factors responsible for such a response in the emphysematous patient is interference with the cleansing mechanism. The patient's protection against "spreads" is enhanced by an effective cleansing mechanism (1) ciliary action, (2) bronchial peristalsis, and (3) cough. Bronchial peristalsis consists not only of changes in the diameter of the bronchial lumen but changes as well in the length of the bronchus during inspiration and expiration. In the overdistended lobe the bronchus is not only distorted by its new position but is relatively fixed and permanently elongated. The amount of foreshortening is reduced. Furthermore, the amount of residual or "stagnant" air is increased and the amount of tidal or "movable" air is reduced. The effective cough is dependent upon movable air. Therefore, not only is overdistention undesirable from a physiologic viewpoint but from a pathologic one as well.

Obliteration of the dead space simultaneous with the segmental resection is done to avoid complications. When an obliterative pleuritis is present the adhesions may prevent the compensatory enlargement of the healthy components and a rather large space remains after the resection of two or more segments. This space may be obliterated in two ways: (1) by a small tailoring thoracoplasty (costectomy), and (2) by extraperiosteal plombage without rib removal.

The small tailoring costectomy removes short segments of second, third, and fourth ribs posteriorly. The first rib may or may not be included. If not, the periosteum on its lower surface is mobilized with the others. The risk of the additional surgery and the paradoxical chest seems justifiable.

The extraperiosteal plombage reduces scoliosis and the amount of paradox. The procedure is the same as described except that the periosteum on the outer surface of the ribs is preserved, the ribs are not removed, and the extraperiosteal "plomb" may consist of (1) the patient's own subscapular collection of blood, (2) many sheets of Gelfoam, or (3) a plastic sponge encased in a polyethylene bag.

In obliterative pleuritis mobilization of the lower and middle lobes is not done when the preoperative fluoroscopy reveals good movement of the diaphragm. Should the lobes be mobilized the diaphragm usually rises to follow their ascent into the thoracic vault. The division of the many adhesions provokes oozing and "sweating" of blood which may result in a hemothorax to bind and restrict diaphragmatic movement. The functional loss from a small tailoring surgical procedure in the thoracic vault is less than that due to diaphragmatic fixation.

STATISTICAL ANALYSIS

A series of 300 consecutive patients who had segmental resection for pulmonary tuberculosis has been followed for one to five years. At the present time 93.7 per cent are living and well, 3.3 per cent living with disease, and 3 per cent are dead (Table I).

TABLE I. DEATHS. 9 (3%)

Primary Operative—3 (1%)	
W. M. 2nd P.O.	? Coronary occlusion
G. A. 4th P.O.	Contralateral pneumonia
W. F. 12th P.O.	Lower nephron nephrosis
Secondary Operative for Bronchopleural fistula—4 (1.3%)	
Other—2 (0.7%)	
A. M. 9 mo. P.O.	of Bronchopleural fistula
G. S. 2 yr. P.O.	of alcoholism

The type of operative procedure was as follows: 210 (70 per cent) had segmental resection only; 32 (10.7 per cent) had lobectomy plus segmental resection; 31 (7 per cent) had bilobar segmental resection; 35 (11.7 per cent) had local excisions only; 2 (0.7 per cent) had right upper and middle lobectomies combined with resection of the superior segment of the right lower lobe. The significant major complications were bronchopleural fistula, tuberculous emphyema, and spread (Table II). In addition one patient had hemorrhage from a small pulmonary vessel and required reopening of the wound for ligation. Another patient required decortication twenty-four days after operation to obtain complete re-expansion of the lung.

TABLE II. 300 SEGMENTAL RESECTIONS. FOLLOWED 1 TO 5 YEARS

Living and well	281 (93.7%)
Living with disease	10 (3.3%)
Dead	9 (3.0%)

There were nine deaths (Table III). Three patients died as a result of the operation. Patient W. A., who was apparently progressing satisfactorily, died suddenly on the second postoperative day presumably from coronary artery disease. Autopsy did not definitely disclose cause of death. Patient G. A. did very well for two days after operation. X-ray review at that time showed clear lung fields, but late in the afternoon of the second day the patient began to show signs of contralateral pneumonia. Death occurred two days later. Post-mortem examination revealed the contralateral lung to be heavy, gelatinous, and essentially free of purulent secretions. Four patients died as a result of secondary operations to correct bronchopleural fistula and tuberculous empyema: M. P. had hemorrhage from a subclavian artery which was involved in the tuberculous empyema. Control was impossible and he died two days later. D. G. died of an anesthetic accident after pneumonectomy had been completed for bronchopleural fistula. L. G. died nine days after

TABLE III. MAJOR COMPLICATIONS

	NO.	DEAD	PERSISTENT	CONTROLLED
Bronchopleural fistula	16 (5.3%)	5 (1.7%)		11 (3.7%)
Empyema	13 (4.3%)	5 (2.7%)	1 (0.3%)	7 (2.3%)
Spread	9 (3%)	5 (1.7%)	1 (0.3%)	3 (1%)

thoracoplasty and partial resection of the right lower lobe to correct bronchopleural fistula. The fistula was controlled but the limited functioning lung tissue was not sufficient to support the patient. F. W. died after multiple procedures to correct fistula which persisted. A. M. died nine months postoperatively with a persistent bronchopleural fistula. An acute bronchitis was the contributing factor to the final episode. G. S. had a segmental resection for tuberculosis and was well with negative culture and clear x-ray films, but he was found dead in bed apparently due to alcoholism two years after operation.

TABLE IV. EXACERBATIONS. 18 (6%)

Resolved	
a. Antibiotics only	5 (1.7%)
b. Additional surgery	6 (2%)
Persistent	7 (2.3%)
Total	18 (6%)

There have been eighteen exacerbations in the entire series (Table IV). Eleven have resolved with further surgery or antibiotic therapy; seven persist. About two-thirds of these occurred immediately or within the first six months and the remainder at scattered later intervals after operation. The late exacerbations have not represented a serious problem in these patients.

Eight patients had planned bilateral resection and two required unplanned contralateral resection for pre-existing disease.

SUMMARY

1. The basic pathology of tuberculosis is an indolent pneumonia which may (1) resolve, (2) fibrose, or (3) caseate. Usually all three elements are present in every lesion.

2. The basic physiology is not significantly changed by segmental resection, because only the diseased components are removed and compensatory mechanisms have already been effected.

3. The indication for segmental or subsegmental resection is a fibrocaseous lesion with or without cavitation confined to one or two segments of a lobe, but still large enough that mature clinical opinion is doubtful of the patient's future security.

4. The preoperative preparation is the same as for any major operation with special attention to laminography and especially the lateral laminography.

5. An anatomic segmental resection is done for moderate and far-advanced lesions. In minimal lesions a wedge resection or local enucleation is possible. Subsegmental resections may also be done anatomically.

6. Postoperative care must be vigilant. Patent airways (intratracheal suction), the control of pain, the use of antibiotics, the obliteration of dead space by complete re-expansion of the lung using active suction and checked by frequent postoperative x-ray examinations are important to a successful result.

7. Tuberculosis is usually bilateral though not bilaterally active. Only the major active focus is removed by segmental resection. The importance of other foci is dependent upon the size and location. Anterior foci are less hazardous than those posteriorly.

8. The problem of overdistention is not great after segmental resection, but obliteration of the dead space is essential to success. Occasionally a periosteal plombage procedure without resection of the ribs is done in deference to this principle.

9. In obliterative pleuritis mobilization of the lung is not done when the preoperative fluoroscopy reveals good diaphragmatic movement. The functional loss is less if a small tailoring surgical procedure is done in the thoracic vault.

These patients were operated upon by us or members of hospital staffs trained by us in order to standardize the technique. Many cases were done on Dr. Berry's service at Bellevue Hospital, Dr. Miscall's service at Triboro Hospital, and the rest were done at St. Albans Naval Hospital, Halloran Veterans Administration Hospital, Nassau County Sanatorium, Brooklyn Thoracic Hospital, and Doctors Hospital. We are grateful to the medical staffs in these hospitals who were mainly responsible for the selection of these cases and for their management and rehabilitation after surgery.

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DISCUSSION

DR. AARON HIMMELSTEIN, New York.—I should like to review the early complications as compiled by Dr. Vaughan and myself from the records of the chest surgical service at Bellevue Hospital in the resections for tuberculosis from October, 1949, through December, 1952. Some of the segmental resections in that group are in Dr. Chamberlain's group, but they also include some of his cases done after the closing date of his series. Almost all these operations were done by the resident surgeons supervised by a member of the staff.

There are 139 lobectomies or pneumonectomies—101 lobectomies and 38 pneumonectomies. In this group there were eight fistulas, two in the pneumonectomy group, the rest in the lobectomy group. Each fistula usually gave us a problem of spread, and the deaths were in large measure in this group. We had ten spreads and six deaths. There were ninety-four segmentals, sixty-four of which were just segments, fifteen were just wedges, one was a lobe and a wedge, and fourteen were lobe and segments.

We have been more rigid in our criteria for selecting a case as having developed a fistula than Dr. Chamberlain was; we have included the group that he called leaks. However, I think there is a distinct difference between them clinically. Leaks that come from the surface of lung that has been opened up, apparently do not present the oppor-

tunity for gross microbial contamination of the pleural space that is present with a leak at the stump of a bronchus. They do not go on frequently to develop empyema. Clinically I think that has been true and I agree with what Dr. Chamberlain said about these leaks. However, we have included all of them as fistulas, and we have twelve in the group of ninety-four segmentals. Four of those were in the group of lobes and segments and six were in the segments alone. There were two deaths in this group; one was due to a proved pulmonary embolus and the second we presumed was a pulmonary embolus although we have no proof by autopsy. Both were in the early postoperative period.

DR. NORMAN WILSON, Brookline.—I should like to congratulate Dr. Chamberlain and his co-workers, not only for their excellent results but to pay tribute to them as pioneers in the use of segmental resection in the treatment of tuberculosis. We all owe a great debt to them. I should like to tell you of some of the lessons we have learned from studying a large series of resections throughout the years, because I think that even though this is a very successful form of treatment in selected cases of tuberculosis, if that selection is violated, the amount of trouble encountered will be very great. To show what I mean, if we separate in our follow-up series those cases which represent primary surgical treatment early in the course of their disease with intelligent timing with regard to drug treatment, we find that 94 per cent of the segmental resections are well in the follow-up study. But if we take those "second-hand" patients who have had other forms of treatment, who have unexpandable lungs, who have had numerous spreads while lying in bed with unsuccessful thoracoplasties for many years, before segmental resection is used (often times as a salvage procedure) then we find that only 50 per cent in the follow-up study are well.

It would be of interest to me to know what percentage of Dr. Chamberlain's cases are primary and what percentage are secondary. You will note that two of the series of cases discussed here this morning represented almost 100 per cent primary treatment cases and this is reflected in the good results reported in their follow-up studies.

We have tried to develop basic fundamental concepts in approaching this problem. In our experience the fundamental requirements which must be observed when using segmental reaction, if good results are to be anticipated, are as follows: (1) An adequate pulmonary reserve, (2) the offending lesion to be resected is within the unit of lung which one intends to resect be it lobe, segment, or lung, (3) that the surgical approach be the primary approach to the problem, (4) that rest and medical treatment have been used to adequately prepare the patient for this procedure.

If these fundamental concepts are adhered to, the results will be good. If they are violated, results will be bad. You will note how carefully Dr. Chamberlain has used lateral laminography to rule out other offending lesions, and I am sure he considers this to be very important and I agree with him on that point. I think it is extremely important not to translate the results of segmental resection representing such ideally selected cases into the experience of those of you who will have to tackle "second-hand" cases, because the problems are entirely different.

DR. E. J. O'BRIEN, Detroit.—It is not easy to take any exception to such a splendid presentation. You have just heard of seven deaths in a series of 300, which is certainly very small. It is a very difficult paper to discuss because Dr. Chamberlain did not put his neck out very far. He showed us a few roentgenograms of patients who were operated upon, but what amount of disease the other patients in the group of 300 had, he does not say. What is bothering me is that his five-year résumé began long before the use of long-term chemotherapy. I cannot understand it. I know what an excellent surgeon Dr. Chamberlain is and I certainly do not question his results, but it rather adds to the chaos I mentioned this morning. I cannot quite visualize how segmental resections can be used in extensive pulmonary lesions without long-term chemotherapy and have such results as he quotes, and I cannot understand either how he differentiates spreads from reactivations. The mere fact that the preoperative film did not show these lesions does not mean a thing to me, because there are many lesions found at the operating table that were not suspected

preoperatively. And it is in these areas that we have frequently seen reactivation. Seven deaths are not very many, but we do not know that any of these were necessary. I showed 403 cases this morning without any treatment other than chemotherapy, and there were no deaths; just five reactivations and two of those had no change in the x-ray appearance. They were called reactivations because of one or two positive cultures which could not be verified after long rehospitalization.

I would like to repeat once more what I said this morning, that the results from resection of so-called "nubbins," as I described small residues after long-term chemotherapy, are meaningless, and I should like to know how many of his patients had or would have had "nubbins" if chemotherapy had been used in continuous long-term treatment previous to resection. We cannot know what would have happened to such lesions had they not been disturbed.

But it is an interesting paper, or what we have heard of it was, and I certainly want to congratulate him on the results if they were obtained from active disease without long-term chemotherapy. I wish I were that good a surgeon.

DR. CHAMBERLAIN (Closing).—Dr. Himmelstein made a good point on fistulas. If we added our "late leaks" to the bronchial fistulas that we had, our figures would be essentially the same, approximately 10 per cent. In other words, we had 6 per cent bronchial fistulas and about the same number of "late leaks," 10 to 12 per cent in all.

Dr. Norman Wilson made some excellent points. We have come to the same conclusion, that whenever the indications for segmental resection are extended we were likely to get into trouble. As I pointed out, the majority of the patients who died had diffuse disease and poor functional reserve. We were trying desperately to salvage these patients by a minimal-sized operation for a maximum amount of disease. The operation cannot be extended too far. It is a segmental operation by name and the disease must be segmental in distribution.

Dr. O'Brien make two very excellent points. When we started this study we did not have chemotherapy, and at St. Albans Hospital we did twenty-six consecutive cases without chemotherapy. We found that those cases, in comparison with a similar number at Halloran Hospital, gave us essentially the same results. But that does not prove too much becaue they were carefully selected cases. This operation is not a dangerous one if the indications are proper. We are the first to admit that only the essential focus is removed and that we must attend carefully to the basic principles of postoperative management, such as obliteration of dead space by maintaining re-expansion. Because we know postoperative management, we are not hesitant to operate upon patients whose organisms have developed resistance to the antibiotics. We believe that antibiotics are no substitute for the basic principles of surgical management.

Dr. O'Brien's other point was an excellent one, too. I am inclined to agree with him in his differentiation of spreads and reactivations. He has made an astute observation. We all know we cannot see all the foci in the x-ray films that we discover at operation and probably some of the lesions we have called spreads may have been reactivations. If you wish, then the spreads may simply be added to the reactivations to get the total figure.

ELECTROLYTE STUDIES IN PERICARDIAL RESECTION

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ALTHOUGH not the first to perform decortication of the heart, Schmieden[1] was early to acquire an experience with the procedure, and in 1926 recommended a regimen of dehydration by limitation of fluid intake and aspiration of pleural fluid in the preparation of such patients for surgery. Subsequently others have advised the preoperative removal of excessive fluid accumulations, some by more vigorous measures which have included the use of diuretics and a rigid restriction of sodium intake.[2-7]

It is not surprising that attempts to rid the body of a substance so important to homeostasis as sodium[8, 9] might occasionally work to a disadvantage, and such a situation arising during the treatment of congestive heart failure has been described and recently named "the low salt syndrome."[10] Peters[11] has pointed out that with a low concentration of sodium in the extracellular fluid, the cells of the tissues take up water and secondary disorders occur, chief of which is circulatory failure. He has also observed and emphasized that ill effects from sodium depletion can occur in the presence of edema, when the concentration of sodium in the serum and extracellular fluids is low, and even when the total quantity of sodium in the body may be excessive.

While performing certain metabolic and physiologic studies on two patients before, during, and after pericardial resection for constrictive pericarditis, we were amazed to find that one, a chronically ill, little 54-year-old man with advanced pulmonary silicotuberculosis, tolerated the operation well, while the other, aged 27 years, previously vigorous, but still muscular and strong in appearance, had a period of hypotension and oliguria for two days after operation and was generally slow to recover although his ultimate result was excellent. In reviewing our observations we have been chiefly impressed by the fact that though both men demonstrate evidence of a disturbed sodium metabolism, the aberrations were more severe in the younger man, and we believe they contributed considerably to the postoperative instability of his circulatory system.

METHODS

The patients were studied on the Metabolic Service during the "balance" period. Fluid intake and urinary output were carefully supervised. Standard techniques in metabolic studies were employed.[12] All food was prepared and served by the metabolic dietitian, refusals were weighed, their contents calculated

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and subtracted from the daily intake. The contents of the daily food intake for various constituents were calculated from acceptable tables.[13-16] Check analyses were performed and these agreed with the calculated values within acceptable limits.[12] The patients were weighed daily in the fasting state. Individual urine specimens were voided into chemically clean Erlenmeyer flasks and pooled into twenty-four hour specimens which were kept under toluene and refrigeration until analysis could be accomplished. Urine, serum, and thoracentesis fluid sodium were determined by gravimetric procedure[17] and flame photometry; urine, serum, and thoracentesis fluid potassium by a titrimetric procedure[18] and flame photometry; urinary nitrogen by the macro-Kjeldahl method[19]; serum chloride by titrimetric means[20,21] serum bicarbonate by the manometric Van Slyke method[22]; hematocrit by the method of Wintrobe[23] corrected[24]; specific gravity of blood and plasma by the copper sulfate method[25]; blood, cell, and plasma volumes were determined with T-1824[26] and the hematocrit. Serum proteins and thoracentesis fluid protein were determined by sodium sulfate precipitation and micro-Kjeldahl nitrogen determination.[27]

"Balance" as here used is the output of a constituent in relation to its intake for a twenty-four hour period. The intake is the sum of oral and parenteral intake (see later material for blood); the output is the sum of urinary output, loss through vomitus, estimated blood loss at operation and by removal of blood for analysis; fecal output, losses through sweating, insensible loss are not included. Neither patient had diarrhea; both operations were performed during cool weather. The volume of blood loss at operation was estimated; the blood loss by venipuncture for analysis was measured. The method of Moore and Ball[28] was used to calculate the amount of sodium, potassium, and nitrogen which transfusions and blood losses contributed to the "balances." The concentration of the various constituents lost by all blood losses was calculated on the basis of the following: a hematocrit of 44 per cent, a cell sodium content of 12.7, a cell potassium content of 103.6, and a cell chloride content of 48.2 meq. per liter; a serum sodium content of 140.8, a serum potassium content of 4.0, and a serum chloride content of 104.1 meq. per liter. These values are based on analyses performed in our laboratory on "normal" blood by one of us (A. Y.).[29] Thus, 1,000 ml. of blood lost would contain in the red blood cells of this liter: sodium 6 meq., potassium 46 meq. and chloride 21 meq.; in the serum, 83 meq. sodium, 2 meq. potassium and 59 meq. chloride.

The amounts of the various constituents given by transfusion of bank blood (blood + ACD solution) were calculated from analysis of two representative samples of bank blood. The average values of these analyses were: hematocrit 41 per cent, plasma sodium 47, cell sodium 6, plasma potassium 5, cell potassium 17, plasma chloride 21, and cell chloride 15 meq. per transfusion unit (average 565 ml.).

In computing fluid intake and output, blood loss was not included because the amounts withdrawn for various tests were relatively small, and the estimated operative blood loss was replaced by transfusion.

The amount of the various constituents lost in the thoracenteses was calculated from analyses in most instances, in a few, the amount of sodium and

potassium was calculated from average values of the Donnan ratios, serum concentrations, and assumed "normal" water concentration of the serum.[30]

Venous pressures were determined according to the procedure of Lyons and his associates.[31] Arm-to-tongue circulation time was done in duplicate using 3 c.c. of 20 per cent sodium dehydrocholate intravenously.

CASE REPORTS

CASE 1.—D. T., a 27-year-old game warden, was admitted Sept. 19, 1949, for the surgical relief of constrictive pericarditis. Previously healthy, one year and a half before he had developed an acute pericarditis with effusion for which he was first admitted. Followed closely since, he improved slowly over a period of several months, and was able to return to work with some restriction of activity. Six months prior to operation, dyspnea and edema recurred and progressed, eventually requiring hospitalization. There was a right pleural effusion, elevated venous pressure (295 cm. water), an enlarged liver, ascites, and heart of normal size with diminished movement. Fibrous constriction appeared to be developing. Decortication was recommended but deferred by the patient. Bed rest, diuretics, a limited salt intake (2 Gm. sodium chloride or 34 meq. sodium per day), and a right thoracentesis (1 L.) effected a weight loss of 9.5 kilos (21 pounds.) in six days to 80.8 kilos. The patient went home on the same low sodium diet to which, with two admitted infractions, he adhered for the 10-week period prior to operation.

Physical examination revealed a husky, muscular young man who did not appear acutely ill. There was evidence of fluid in the right pleural cavity below posterior D6. The liver was 8 cm. below the costal margin, and there were signs of some free abdominal fluid. There was no peripheral edema. The blood pressure was 120/70, weight 86 kilos (189½ pounds).

Decortication of the heart was performed Sept. 28, 1949, through a left transpleural approach. Pleural adhesions were dense and vascular. All intrapleural and intrapericardial structures were red and swollen, causing a widespread ooze difficult to control, resulting in more than the ordinary loss of blood. Although in the immediate postoperative period he developed hypotension and oliguria, later convalescence was satisfactory, and now, four years later, he works strenuously as a game warden and denies any physical limitation whatsoever.

CASE 2.—J. L., a 54-year-old man, was admitted Dec. 8, 1949, because of anorexia, weight loss, and fever. He had worked as a sandblaster and stone cutter for thirty-five years, most of the time without adequate protection. After a chest film four years before he was told he had "spots on his lungs." Four months prior to admission he was acutely ill with substernal pain and fever of 105° F. A diagnosis of acute pericarditis was made at another hospital. Two months before admission he became jaundiced and developed upper abdominal discomfort, chiefly after eating; this resulted in a loss of appetite. After two weeks the jaundice cleared but the other symptoms persisted and an evening fever was detected.

Physical examination revealed a chronically ill, poorly developed, and poorly nourished little man who looked considerably older than his stated years. The neck veins were engorged. There was dullness at the right base below the angle of the scapula. The liver was 8 cm. below the costal margin. There was induration, enlargement, and tenderness of the lower pole of the left epididymis. Both lobes of the prostate were indurated and fixed. There was a nontender, firm, nodular, mobile mass in the region of the left seminal vesicle. The blood pressure was 108 to 120/90, paradoxical, weight 57 kilos (125¾ pounds).

Laboratory Data.—Hemogram was within normal limits, sedimentation rate 19 mm. per hour (Westergren); venous pressure was elevated to 240 mm. of saline. Roentgen examination of the chest showed disseminated nodular densities throughout both lung fields with numerous small calcifications and pleural thickening at the right base. At the right apex there was an increase and some confluence of the nodularities suggesting an active tuberculous process. On fluoroscopy cardiac pulsations were diminished. Excretory urograms were normal except for elevation of the bladder floor consistent with prostatic enlargement. Sputum and urine cultures were positive for tubercle bacilli.

He was digitalized without loss of weight and after five days this medication was discontinued. On a low salt diet (2 Gm. sodium chloride) and mercurials he lost 5.5 kilos in one week. He required one mercurial injection a week to maintain this weight level. Streptomycin, 1 Gm., was begun Feb. 21, 1950, and given daily for 120 days. Pericardial resection by a left transpleural approach was performed on February 27, and a satisfactory decortication obtained. The patient tolerated the procedure well and immediate convalescence was uneventful although ultimate rehabilitation has been poor because of senescence, silicotuberculosis, and limited movement of the left shoulder associated with pain in the thoracotomy wound.

CLINICAL OBSERVATIONS

The immediate response of the two men to operation was in direct contrast to their general appearance. D. T., the young game warden, came to the operating room with his normal blood pressure of 120 to 125/80 to 90 mm. mercury depressed by preoperative medication to 100/65. It returned to the normal level following induction, but after one hour and a half began to rise in stages, reaching 150/90 about an hour later; it remained at that level for forty-five minutes then began a gradual decline over the next six hours, falling below 100/60 as he left the operating room to an unstable range of 50 to 60/30 to ?? (Fig. 1). In spite of four blood transfusions hypotension developed and persisted for forty-eight hours. The night following operation was particularly critical. The margin between shock and pulmonary edema was so narrow that despite every effort and attention of the staff he developed both. There was oliguria to the extent that only 55 c.c. were produced the day of operation, 335 c.c. the day following, and 975 c.c. the next day in spite of corresponding fluid intake of 3,850 c.c., 7,700 c.c. and 5,430 c.c. (Table II).

The possibility that a deficiency of sodium was a factor in this complex clinical picture was considered at the time, and during the first night 1,720 c.c.

of physiologic saline was given between midnight and morning (Fig. 1). Although the blood pressure level improved, the development of pulmonary edema necessitated discontinuance of the venoclysis for about four hours. On the first postoperative day, he was given 1,900 c.c. of physiologic saline and took some fluids by mouth, receiving 310 meq. of sodium that day, still without stabilizing his blood pressure. On the second postoperative day he was given 2,000 c.c. of saline containing 310 meq. of sodium. Late in the afternoon, the serum sodium level on blood drawn that morning was reported to be 123.2 meq. per liter.

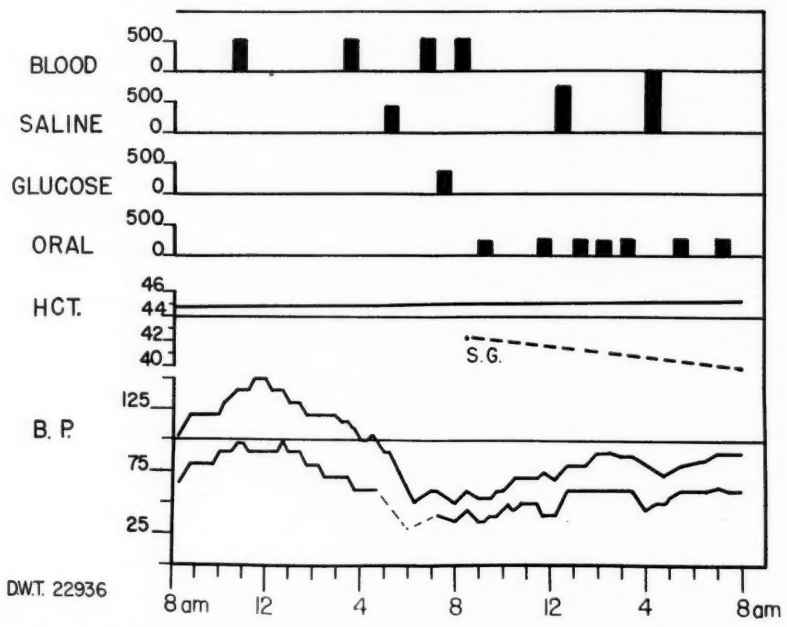

Fig. 1.—The blood pressure, hematocrit, and fluid intake of the patient in Case 1 for the operative day starting at 8:00 A.M. HCT = hematocrit; S. G. = hematocrit determined from the specific gravity of blood and plasma. (See reference 25.)

It was then decided to give hypertonic saline, and 200 c.c. of a 4 per cent solution of sodium chloride containing 123 meq. of sodium was injected by intravenous drip. From the clinical standpoint this was the turning point in the course. The patient soon looked and felt much better, the blood pressure became more stable, and he was not hypotensive again. Urine volume increased during the night and was copious the next day (Fig. 4, and Table II).

J. L., the frail elderly man with silicotuberculosis, came to the operating room with his normal blood pressure of 100 to 110/70 to 80 essentially unchanged. Following induction it stabilized at 120/90, where it remained for two hours before declining to 100/80; he responded to transfusion after an hour and left the operating room at a level of 110/70. During the next twenty-

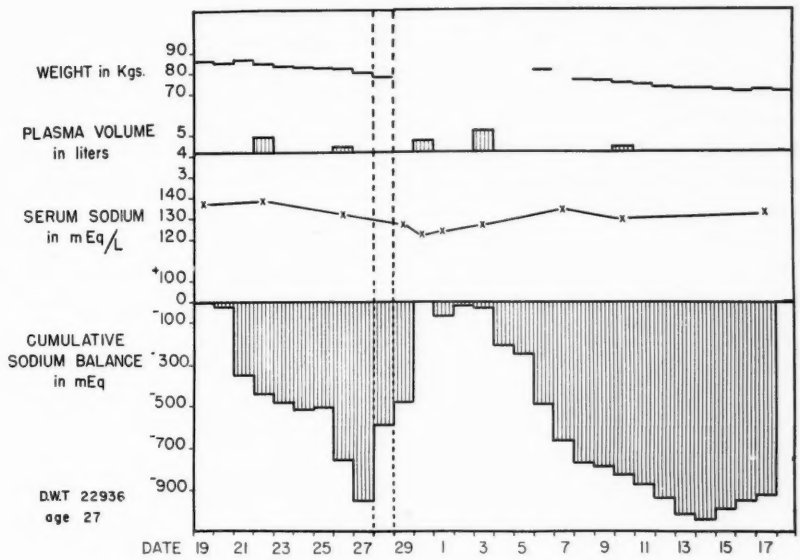

Fig. 2.—Cumulative sodium balance, serum sodium, plasma volume, and weight of the patient in Case 1. The operative day is denoted by the vertical broken lines. For explanation of cumulative "balance," see text.

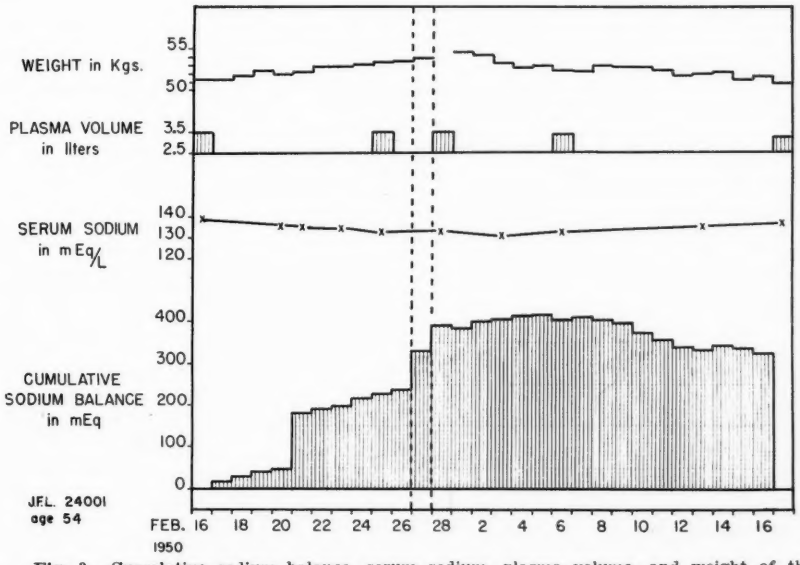

Fig. 3.—Cumulative sodium balance, serum sodium, plasma volume, and weight of the patient in Case 2. The operative day is denoted by the vertical broken lines. For explanation of the cumulative "balance," see text.

four hours his condition was good and continued to improve. The blood pressure ranged over 105 to 120/80 to 60, never dropping below 100 systolic. Urine output was 630 c.c. the day of operation (all postoperative) and 1,000 c.c. and 1,175 c.c. the two following days (Table III).

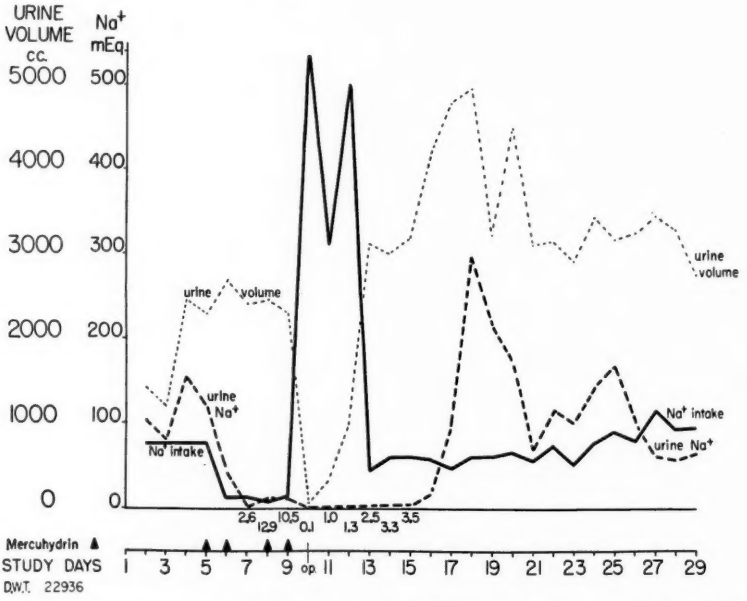

Fig. 4.—Urine volume, daily urinary sodium excretion, and daily sodium intake of the patient in Case 1. The operative day and the days of Mercuhydrin Sodium Solution administration are noted at the bottom of the figure.

LABORATORY OBSERVATIONS

Data obtained are arranged in tabular form and presented in Tables I to VII. See pages 495 to 500.

The most striking difference between the two cases, in which Case 1 compared unfavorably, was in the metabolism of sodium. This is brought out most forcefully by adding and subtracting the day to day sodium balances of each of the men and presenting the excess or deficit from the beginning of the balance study to any one day in the study period as a simple figure of sodium credit or debit (Figs. 2 and 3 and Table I).

It can be seen that whereas the patient Case 2 had within his body on the morning of operation some 240 meq. of sodium more than at the beginning of the study, the patient in Case 1 came to the operation with 950 meq. of sodium less. Both men were on low sodium diets and had been for two months prior to the study. Whereas the patient in Case 2 excreted little sodium in urine, suffered no major losses, and was able to gain 150 meq. during a test of renal function with sodium hippurate, the patient in Case 1 did not effect at first any renal

conservation and lost 750 meq. of sodium (44 Gm. of salt) in three chest taps. There was an associated loss of 8 kilos (17½ pounds) body weight (Tables II and III). Repeated thoracenteses following operation produced a further loss of 590 meq. of sodium and on one occasion, the first postoperative day, accounted for a loss of nearly 200 meq. of sodium when an attempt was being made to treat sodium deficiency by giving 300 meq. intravenously, resulting in a net gain to the body that day of only 100 meq. of sodium.

A comparison of the daily urinary sodium excretion patterns in these two patients reveals the following: 1. the patient in Case 1 was initially excreting more sodium than he took in and this occurred at a relatively "normal" level

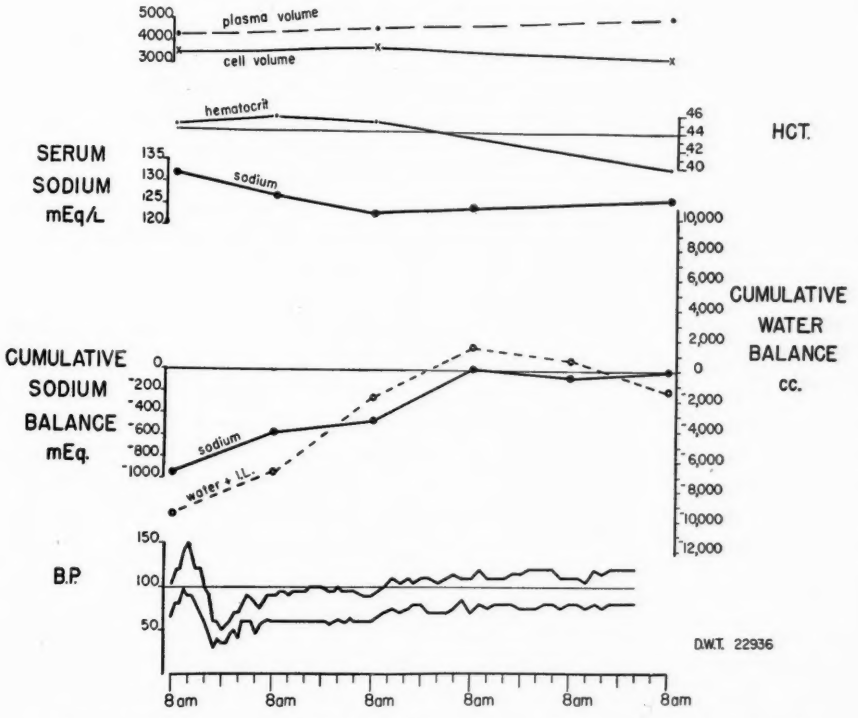

Fig. 5.—Blood pressure, cumulative sodium balance, cumulative water balance, serum sodium concentration, hematocrit, cell volume, and plasma volume of the patient in Case 1; the observations start on the day of operation and include the first four postoperative days. Cumulative water balance is computed from measurement of the fluid intake and output with an additional allowance of 700 c.c. (afebrile) daily insensible loss before operation and 1,000 c.c. (febrile) after operation.

of intake. The patient in Case 2 excreted insignificant amounts of sodium on a "low" intake, and this remained constant throughout the preoperative period, with the exception of the clearance day. 2. The patient in Case 1 decreased daily sodium urinary output when intake was markedly reduced, but these levels were never so low as those in Case 2 on approximately the same level of

intake. The response was undoubtedly influenced by the administration of diuretics. 3. The operative day in both patients is characterized by very low levels of sodium output in relation to intake. However, the patient in Case 1 manifested an anuria, 55 c.c. output, while the patient in Case 2 showed only a reduction of urine volume from the preoperative level. 4. During the first five and four days after operation, both patients showed reduced daily urinary sodium excretion.

Data relative to the potassium "balances" in these patients will be found in Tables IV and V. There was a slightly negative potassium balance immediately before operation in Case 1 in contrast to Case 2 which was in a slightly positive potassium balance. On the operative day, the patient in Case 1 showed a slightly positive balance, because of anuria and transfusions, while the patient in Case 2 showed a negative balance. After operation, the immediate potassium balance was positive in Case 1 and negative in Case 2. The patient in Case 1 then remained in a slightly negative potassium balance in contrast to the patient in Case 2 who returned to a slightly positive balance. The potassium balance in Case 2 is more typical of that encountered in patients undergoing a similar degree of surgical trauma than is the balance in Case 1.[28] The pattern of the potassium balance in the patient in Case 1 with a normal serum potassium in the immediate postoperative course would appear to rule out potassium depletion as an important etiological factor contributing to the abnormalities of the postoperative course. The serum potassium of the patient in Case 2 reached its lowest levels at a time when the positive potassium balance was being established.

Data relative to the nitrogen balance in both patients are given in Tables IV and V. There was a negative nitrogen balance in Case 1 immediately before operation which was in part due to a therapeutic change in diet and nitrogen loss as protein in the thoracenteses. On the operative day the patient was in nitrogen equilibrium with a very low urine output. There then followed seven days of negative balance with impaired kidney function, elevated blood NPN, diminished urine output on an adequate fluid intake, and nitrogen loss in thoracenteses. This in turn was succeeded by eleven days of approximate nitrogen equilibrium, the balance becoming definitely positive on the last study day. This illustrates the role of the removal of protein nitrogen by thoracenteses in contributing to negative nitrogen "balance." In contrast, the balance in the patient in Case 2 was positive before operation, was definitely negative on the operative day, and remained negative for four days, becoming positive on the fifth day and remaining so throughout the remainder of the study. The pattern of his nitrogen balance was considered typical of a patient undergoing a surgical procedure of this degree.[28]

Serum and blood constituents, blood and plasma volumes, circulation time and venous pressure during and after the metabolic study period are presented in Tables VI and VII. Both men had abnormally low serum sodium levels at

some time (normal 135 to 145 meq. per liter). However, the patient in Case 1 was definitely subnormal two days prior to operation, reached a quite low level (123.2 meq. per liter) two days after operation, and was persistently below normal over a span of four weeks.

In Case 1, the nonprotein nitrogen values were moderately elevated during the immediate postoperative period, associated with a low urine output.

Blood and plasma volumes obtained during the study period were normal or above[32] at all times in both patients. One such determination obtained in Case 1 two days after operation, when he was still hypotensive, was above normal values for a man of his weight range. Moreover, on other occasions when he was clinically much improved he had lower values of both blood and plasma volumes.

The venous pressure of the patient in Case 1 was high before operation and showed a good response to the procedure. On the other hand, the patient in Case 2, whose venous pressure was not so high prior to operation, had no drop at first, and though ultimately declining it did not reach a similar low level.

TABLES I TO VII

TABLE I. CASES 1 AND 2. COMPARISON OF CUMULATIVE SODIUM "BALANCES"

DATE 1949	CASE 1 CUMULATIVE "BALANCE" MEQ.	CASE 2 CUMULATIVE "BALANCE" MEQ.	DATE 1950
9/18		+18.1	2/17
9/19		+29.6	2/18
9/20	−27.1	+41.2	2/19
9/21	−354.9	+47.8	2/20
9/22	−443.2	+180.6	2/21
9/23	−486.7	+191.9	2/22
9/24	−517.1	+196.5	2/23
9/25	−507.4	+216.4	2/24
9/26	−757.2	+225.6	2/25
9/27	−951.9	+237.0	2/26
Operation 9/28	−586.1	+329.0	2/27
9/29	−483.9	+390.3	2/28
9/30	+1.0	+385.3	3/1
10/1	−70.8	+399.8	3/2
10/2	−14.8	+405.1	3/3
10/3	−27.3	+413.9	3/4
10/4	−208.1	+415.7	3/5
10/5	−256.6	+404.0	3/6
10/6	−491.7	+410.0	3/7
10/7	−662.1	+402.5	3/8
10/8	−770.5	+395.1	3/9
10/9	−784.1	+373.5	3/10
10/10	−824.7	+350.2	3/11
10/11	−872.8	+339.5	3/12
10/12	−937.6	+323.8	3/13
10/13	−1015.6	+335.3	3/14
10/14	−1038.6	+329.9	3/15
10/15	−988.2	+320.6	3/16
10/16	−953.1		
10/17	−922.9		

For explanation of cumulative "balance," see text.

TABLE II. CASE 1

	FLUID "BALANCE"						SODIUM "BALANCE"					
DATE 1949	WGT. KILOS.	FLUID INTAKE C.C.	URINE VOLUME C.C.	LOSS CHEST TAPS C.C.	TOTAL FLUID LOSS C.C.	"BALANCE" C.C.	TOTAL INTAKE MEQ.	LOSS CHEST TAPS MEQ.	LOSS BLOOD MEQ.	LOSS URINE MEQ.	TOTAL OUTPUT MEQ.	"BALANCE" MEQ.
9/20	85.9	2430	1415		1415	+1015	77			104.1	104.1	−27.1
9/21	86.2	1230	1195	2347	3542	−2310	77	322.2		82.6	404.8	−327.8
9/22	84.3	2940	2450		2450	+490	77		10	155.3	165.3	−88.3
9/23	83.6	2810	2285		2285	+525	77			120.5*	120.5	−43.5
9/24	83.1	2720	2670		2670	+50	12.3			42.7*	42.7	−30.4
9/25	82.8	2140	2400		2400	−260	12.3			2.6	2.6	+9.7
9/26	82.2	2620	2445	1800	4245	−1625	8.9	235.8	10	12.9*	258.7	−249.8
9/27	79.8	1950	2285	1500	3785	−1835	12.3	196.5		10.5*	207.0	−194.7
9/28	77.9	3850	55		55	+3795	533.9		168	0.1	168.1	+365.8
9/29		7700	335	1500	1835	+5865	309.7	196.5	10	1.0	207.5	+102.2
9/30		5430	975		975	+4455	496.2		10	1.3	11.3	+484.9
10/1		3500	3105	900	4005	−505	45.5	109.8	5	2.5	117.3	−71.8
10/2		3450	2990		2990	+460	59.3			3.3	3.3	+56.0
10/3		3955	3170	475	3645	+310	60.8	59.8	10	3.5	73.3	−12.5
10/4		5160	4150	1700	5850	−690	57.0	221.2		16.6	237.8	−180.8
10/5		3470	4750		4750	−1280	47.7			96.2	96.2	−48.5
10/6	81.6	4130	4925		4925	−795	60.1			295.2	295.2	−235.1
10/7		3190	3455	50	3505	−315	61.2	6.7	10	214.9	231.6	−170.4
10/8	76.5	4335	4460		4460	−125	65.5			173.9	173.9	−108.4
10/9	76.2	3620	3070		3070	+550	55.5			69.1	69.1	−13.6
10/10	75.3	4680	3120		3120	+1560	73.3			113.9	113.9	−40.6
10/11	74.5	2990	2890		2890	+100	51.0			99.1	99.1	−48.1
10/12	73.6	4010	3410		3410	+600	76.4			141.2	141.2	−64.8
10/13	72.7	3360	3140		3140	+220	88.7			166.7	166.7	−78.0
10/14	72.6	4070	3230		3230	+840	79.0			102.0	102.0	−23.0
10/15	71.8	4040	3435		3435	+605	114.0			63.6	63.6	+50.4
10/16	71.6	3860	3270		3270	+590	93.0			57.9	57.9	+35.1
10/17	71.8	3710	2740		2740	+970	94.3			64.1	64.1	+30.2

The day of operation is 9/28.

For definition of "balance" and the method of handling losses and gains of the various constituents in blood given and removed in calculation of the "balances" in this and subsequent Tables, see METHODS.

*Mercuhydrin, 2 c.c., administered intravenously.

TABLE III. CASE 2

	FLUID "BALANCE"						SODIUM "BALANCE"					
DATE 1950	WGT. KILOS.	FLUID INTAKE C.C.	URINE VOLUME C.C.	LOSS CHEST TAPS C.C.	TOTAL FLUID LOSS C.C.	"BALANCE" C.C.	TOTAL INTAKE MEQ.	LOSS CHEST TAPS MEQ.	LOSS BLOOD MEQ.	LOSS URINE MEQ.	TOTAL OUTPUT MEQ.	"BALANCE" MEQ.
2/17	51.4	1770	1210		1210	+560	24.1		5.5	0.46	6.0	+18.1
2/18	51.9	1390	1260		1260	+130	11.9			.35	0.4	+11.5
2/19	52.4	1870	1100		1100	+770	11.9			.32	0.3	+11.6
2/20	51.8	2010	1210		1210	+800	11.9		4.9	.39	5.3	+6.6
2/21	52.1	2150	1330		1330	+820	171.1†		10.0	28.3	38.3	+132.8
2/22	52.9	1770	1170		1170	+600	11.9			.62	0.6	+11.3
2/23	52.9	1530	995		995	+535	11.9		6.9	.41	7.3	+4.6
2/24	53.1	1830	855		855	+975	26.5†		6.2	.43	6.6	+19.9
2/25	53.4	1530	965		965	+565	11.9		2.4	.32	2.7	+9.2
2/26	53.5	1530	1175		1175	+355	11.9			.50	0.5	+11.4
2/27	53.8	3980	610		610	+3370	177.8		83.0	2.78	85.8	+92.0
2/28		3620	1020		1380*	+2240	76.4		6.2	3.61	15.1‡	+61.3
3/1	54.6	2235	1295	250	1545	+690	29.0†	25.2	7.5	1.25		−5.0
3/2	54.2	1860	1100		1100	+760	15.0			0.45		+14.5
3/3	53.4	1620	785		785	+835	10.9		4.9	0.69	5.6	+5.3
3/4	52.7	2080	1110		1110	+970	13.0			4.15	4.2	+8.8
3/5	52.9	1500	625		625	+875	9.4			7.6	7.6	+1.8
3/6	52.4	1500	755		755	+745	13.6		7.5	17.8	25.3	−11.7
3/7	52.3	1920	740		740	+1180	28.7†		4.2	18.5	22.7	+6.0
3/8	52.8	1530	875		875	+655	10.4			17.9	17.9	−7.5
3/9	52.7	1630	1240		1240	+390	10.7			18.1	18.1	−7.4
3/10	52.7	1870	1240		1240	+630	9.9			31.5	31.5	−21.6
3/11	52.2	1435	1365		1365	+70	10.3			33.6	33.6	−23.3
3/12	51.6	1630	975		975	+655	11.9			22.6	22.6	−10.7
3/13	52.0	1390	1070		1070	+320	11.9		4.9	22.7	27.6	−15.7
3/14	52.1	2165	1490		1490	+675	29.6†		4.5	14.6	19.1	+11.5
3/15	51.3	1630	1135		1135	+495	11.9			17.3	17.3	−5.4
3/16	51.6	1630	1225		1225	+405	11.9			21.2	21.2	−9.3
3/17	50.9	1390	950		950	+440			7.5	8.6		

See legend Table II for explanation.
The operative day is 2/27.
*Includes vomitus, 360 c.c.
†Includes parenteral sodium given for renal clearance studies.
‡Includes 5.3 meq. sodium lost in vomitus.

TABLE IV. CASE 1

	POTASSIUM "BALANCE"						NITROGEN "BALANCE"					
DATE 1949	TOTAL INTAKE MEQ.	LOSS CHEST TAP MEQ.	LOSS BLOOD MEQ.	LOSS URINE MEQ.	TOTAL OUTPUT MEQ.	"BALANCE" MEQ.	TOTAL INTAKE GM.	LOSS CHEST TAP GM.	LOSS BLOOD GM.	LOSS URINE GM.	TOTAL OUTPUT GM.	"BALANCE" GM.
9/19			.3						0.7			
9/20	110.1			85.3	85.3	+24.8	25.6			15.1	15.1	+10.5
9/21	109.2	6.0		28.2	34.2	+75.0	25.6	13.7		15.8	29.5	−3.9
9/22	112.2		.3	99.1	99.4	+12.8	25.6		0.7	15.8	16.5	+9.1
9/23	110.1			98.4	98.4	+11.7	25.6			16.2	16.2	+9.4
9/24	59.9			100.2	100.2	−40.3	13.2			15.4	15.4	−2.2
9/25	62.8			58.0	58.0	+4.8	13.2			15.4	15.4	−2.2
9/26	60.7	5.4	.3	76.0	81.7	−21.0	8.3	14.2	0.7	13.2	28.1	−19.8
9/27	59.9	4.5		58.9	63.4	−3.5	13.2	11.8		11.3	23.1	−9.9
9/28	20.0		4.0	5.4	9.4	+10.6	11.2		11.2	0.5	11.7	−0.5
9/29	53.1	5.0	.3	20.5	25.8	+27.3	4.7	9.9	0.7	1.9	12.5	−7.8
9/30	14.9		.3	44.4	44.7	−29.8	3.0		0.7	7.6	8.3	−5.3
10/1	37.9	3.3	.1	64.5	67.9	−30.0	8.3	3.8	0.4	21.0	25.2	−16.9
10/2	71.1			62.4	62.4	+8.7	12.1			24.3	24.3	−12.2
10/3	64.7	1.9	.3	56.9	59.1	+5.6	14.1	1.8	0.7	18.5	21.0	−6.9
10/4	57.6	6.6		78.4	85.0	−27.4	13.2	9.5		18.9	28.4	−15.2
10/5	66.0			87.0	87.0	−21.0	14.5			18.1	18.1	−3.6
10/6	77.4			92.7	92.7	−15.3	17.7			18.2	18.2	−0.5
10/7	76.6	0.2	.3	86.9	87.4	−10.8	17.2	0.2	0.7	13.9	14.8	+2.4
10/8	93.2			124.5	124.5	−31.3	21.7			20.2	20.2	+1.5
10/9	57.2			88.3	88.3	−31.1	11.0			15.8	15.8	−4.8
10/10	98.2			117.9	117.9	−19.7	19.7			20.6	20.6	−0.9
10/11	78.0			81.8	81.8	−3.8	17.4			17.8	17.8	−0.4
10/12	84.8			91.6	91.6	−6.8	19.9			19.4	19.4	+0.5
10/13	88.3			93.4	93.4	−5.1	17.8			18.9	18.9	−1.1
10/14	85.5			94.8	94.8	−9.3	19.8			19.3	19.3	+0.5
10/15				71.6	71.6		18.5			18.0	18.0	+0.5
10/16				84.6	84.6		20.1			19.8	19.8	+0.3
10/17				71.2	71.2		23.8			16.0	16.0	+7.8

For explanation see Table II.
The operation day is 9/28.

TABLE V. CASE 2

	POTASSIUM "BALANCE"						NITROGEN "BALANCE"					
DATE 1950	TOTAL INTAKE (MEQ.)	LOSS CHEST TAPS (MEQ.)	LOSS BLOOD (MEQ.)	LOSS URINE (MEQ.)	TOTAL OUTPUT (MEQ.)	"BALANCE" (MEQ.)	TOTAL INTAKE (GM.)	LOSS CHEST TAPS (GM.)	LOSS BLOOD (GM.)	LOSS URINE (GM.)	TOTAL OUTPUT (GM.)	"BALANCE" (GM.)
2/17	80.0			60.4	60.4	+19.6	15.4			12.0	12.0	+3.4
2/18	84.0			72.0	72.0	+12.0	15.3			13.8	13.8	+1.5
2/19	84.0			55.0	55.0	+29.0	15.4			10.8	10.8	+4.6
2/20	79.5			69.1	69.1	+10.4	15.1			11.9	11.9	+3.2
2/21	85.5		0.2	102.4	102.6	−17.1	15.3		0.5	14.2	14.7	+0.6
2/22	82.2			60.0	60.0	+22.2	15.4			13.1	13.1	+2.3
2/23	78.0		0.2	55.0	55.2	+22.8	15.1		0.5	12.8	13.3	+1.8
2/24	85.6			56.6	56.6	+29.0	15.3			11.0	11.0	+4.3
2/25	82.2			57.3	57.3	+24.9	15.4			11.8	11.8	+3.6
2/26	77.5			63.1	63.1	+14.4	12.8			11.9	11.9	+0.9
2/27	15.0		2.0	71.4	73.4	−58.4	8.1		5.0	7.7	12.7	−4.6
2/28	42.6	2.4*		62.1	64.5	−21.9	4.7			9.6	9.6	−4.9
3/1	32.6	0.7	0.2	42.7	43.6	−11.0	3.4	1.9	0.5	11.5	13.9	−10.5
3/2	35.0			23.7	23.7	+11.3	4.9			8.3	8.3	−3.4
3/3	35.1			24.6	24.6	+10.5	5.7			6.9	6.9	−1.2
3/4	47.6			36.4	36.4	+11.2	8.5			8.1	8.1	+0.4
3/5	58.8			36.0	36.0	+22.8	8.3			7.5	7.5	+0.8
3/6	53.0		0.2	39.3	39.5	+13.5	10.8		0.5	8.7	9.2	+1.6
3/7	43.8			35.6	35.6	+8.2	9.5			8.1	8.1	+1.4
3/8	47.5			40.5	40.5	+7.0	9.7			9.5	9.5	+0.2
3/9	59.6			46.5	46.5	+13.1	11.3			9.6	9.6	+1.7
3/10	72.6			52.0	52.0	+20.6	12.8			8.3	8.3	+4.5
3/11	71.5			66.3	66.3	+5.2	12.6			10.6	10.6	+2.0
3/12	82.0			65.6	65.6	+16.4	15.3			10.6	10.6	+4.7
3/13	79.6			84.1	84.1	−4.5	15.1			12.3	12.3	+2.8
3/14	84.2			69.0	69.0	+15.2	15.4			11.7	11.7	+3.7
3/15	78.2			64.4	64.4	+13.8	15.0			12.1	12.1	+2.9
3/16	79.2			82.4	82.4	−3.2	15.1			13.5	13.5	+1.6
3/17	84.2			55.6	55.6	+28.6	15.4			11.0	11.0	+4.4

For explanation see Table II.
The day of operation is 2/27.
*Vomitus, 360 c.c.

TABLE VI. CASE 1. SERUM AND BLOOD CONSTITUENTS, BLOOD AND PLASMA VOLUMES, CIRCULATION TIME, AND VENOUS PRESSURE

	SERUM						BLOOD						
DATE 1949	SODIUM (MEQ./L.)	POTASSIUM (MEQ./L.)	CHLORIDE (MEQ./L.)	ALBUMIN (GM. %)	GLOBULIN (GM. %)	TOTAL PROTEINS (GM. %)	NPN (MG. %)	HEMATOCRIT (%)	BLOOD VOLUME (C.C.)	PLASMA VOLUME (C.C.)	RED CELL VOLUME (C.C.)	CIRC. TIME (SEC.)	VENOUS PRESSURE (MM. SALINE)
9/19	136.9	4.2	106.0	4.4	2.8	7.2	35	42.9				34	320
9/22	138.6	3.4	104.0	3.8	2.2	6.0	29	42.8	8741	5000	3741	37	350
9/26	132.0	4.0	99.5	3.6	3.2	6.8		44.6	7865	4357	3508	32	295
9/29	127.1	4.4	96.6	3.5	2.5	6.0	50	45.7					
9/30	123.2	4.9	94.8	3.8	2.6	6.4	56	45.1	8599	4721	3878		
10/1	124.3	4.8	96.0	4.2	2.0	6.2	66						
10/3	126.6	5.2	98.0	3.1	2.6	5.7	39	39.7	8662	5223	3439		
10/7	134.7	5.4	99.9	3.4	2.8	6.2	30						
10/10	129.8	3.4	100.0	3.3	4.1	7.4	34	38.3	7164	4420	2744	18	165
10/12		3.4		3.6	4.0	7.6							
10/17	131.5	3.8		3.5	4.6	8.1	29	39.8				20	92
10/24	134.4		98.5	3.5	3.8	7.3	28	39.0					
11/30	135.7	3.9	101.9	3.9	4.0	7.9	29						
3/8/50	138.3	5.1	99.0	4.5	2.5	7.0	37	47.5	8080	4247	3833		

The operative day is 9/28.

TABLE VII. CASE 2. SERUM AND BLOOD CONSTITUENTS, BLOOD AND PLASMA VOLUMES, CIRCULATION TIME, AND VENOUS PRESSURE

	SERUM							BLOOD						
DATE 1950	SODIUM (MEQ./L.)	POTASSIUM (MEQ./L.)	CHLORIDE (MEQ./L.)	BICARBONATE (MEQ./L.)	ALBUMIN (GM. %)	GLOBULIN (GM. %)	TOTAL PROTEINS (GM. %)	NPN (MG. %)	HEMATOCRIT (%)	BLOOD VOLUME (C.C.)	PLASMA VOLUME (C.C.)	RED CELL VOLUME (C.C.)	CIRC. TIME (SEC.)	VENOUS PRESSURE (MM. SALINE)
2/16	139.4	3.9	104	24.2	3.7	4.6	8.3	33	43.1	6134	3490	2644		
2/17									43.0				32	200
2/20	136.3	4.2	105	23.1	3.6	4.6	8.2	34	45.5					
2/21	135.5								43.8				23	167
2/23	134.4	4.0	103	24.1	3.3	4.3	7.6		41.0					
2/24								36	41.4					165
2/25	132.5								39.9	5834	3506	2328		
2/28	133.1	3.6	101	17.8	3.5	3.7	7.2	41	40.4	5815	3466	2349	22	180
3/1									42.2					
3/3	130.8	3.3	97	19.3	3.4	4.0	7.4	33	43.7					
3/4													20	175
3/6	132.4	3.0	98	20.4	3.7	4.0	7.7	34	43.7	6406	3404	3002		
3/13	134.9	4.0	101	22.3	3.4	4.5	7.9	29	41.5				26	182
3/14													18	130
3/17	136.0				2.8	5.2	8.0	33	41.9	5718	3322	2396		

The operative day is 2/27.

DISCUSSION

Sodium depletion is usually accompanied by dehydration, and circulatory failure is recognized as an important clinical feature of this condition.[9, 33-36] In experimental salt depletion in animals it has been demonstrated that the circulatory impairment is due chiefly to a lowered plasma volume secondary to shrinkage of extracellular fluid but is also unfavorably influenced by the presence of hyponatremia.[37-41] With the increasing use of intravenous saline-free fluids[42-44] and the application of regimens of sodium restriction to the treatment of edematous states, particularly those of a cardiovascular nature,[10, 45, 46] instances are encountered in which a sodium deficiency exists in the absence of dehydration and when there may be an increase of the total amount of sodium in the body.[10, 11, 47-49] Hyponatremia is seen in the presence of edema. In this situation the pathogenesis of the circulatory impairment is not clearly understood, but Peters[11] suggests that there may be altered cellular function associated with maldistribution of water within the body.

Features favoring sodium depletion in Case 1 are as follows:

For two months prior to the preoperative study period he had been on a low sodium intake of about 34 meq. per day. In spite of the use of diuretics and a good urine volume there was a low urinary sodium output in the three or four days preceding operation.[50] There was a cumulative deficit of 950 meq. of sodium in the preoperative phase of the study period. Since the average total exchangeable sodium in a 70 kilo man is 2,950 meq.,[51] it can be appreciated that the magnitude of such a deficit occurring in eight days is considerable. In the latter part of the second postoperative day there was clinical improvement which coincided with the correction of the deficiency by hypertonic saline.

Abnormally low serum sodium levels are considered good evidence for sodium depletion, since with experimental depletion, the level of serum sodium is conserved for a time by loss of water, and then falls when the sodium deficit becomes considerable. Apparently osmotic pressure of the body fluids is first conserved at the expense of volume before yielding to hypotonicity.[9, 44]

It is impossible to indicate or analyze the numerous elements that contributed to the period of hypotension in Case 1. The presence of the constrictive pericarditis with its peculiar physiologic effects undoubtedly influenced the metabolism of sodium and water and modified the classical picture of sodium depletion derived from human and animal experiments. Drugs, anesthesia, stress arising from the mental and physical trauma are but a few of the many factors affecting any patient under these circumstances. However, in the search for tangible evidence to explain why the young man reacted in an almost disastrous manner to the same operative procedure that the older man tolerated well it did not seem that the great difference in sodium metabolism could be ignored.

SUMMARY AND CONCLUSIONS

Metabolic studies have been conducted on two cases of pericardial resection for constrictive pericarditis. A comparison is made between the two in regard to the immediate postoperative course, which was benign in one and stormy in the other. An analysis of data obtained indicates that a preoperative

regimen of sodium restriction and withdrawal may be carried so far as to be deleterious. The following evidence is presented to support this view:

1. During the eight days of balance studies prior to operation, there occurred a cumulative deficit of 950 meq. of sodium (55 Gm. of salt), chiefly through aspiration of pleural fluid.

2. Hyponatremia (123.2 meq. per liter) occurred.

3. Total urinary sodium excretion for the seventy-two hours prior to operation was only 25 meq. despite the repeated use of a mercurial diuretic.

4. Hypotension developed while blood was being received and continued in spite of replacement of the estimated operative blood loss. Values for hematocrit and blood and plasma volume obtained during the period of hypotension did not indicate the presence of inadequately treated hemorrhage.

5. Hypotension and oliguria were overcome at about the time the sodium deficit was corrected.

In preparing cardiac patients for surgery the possibility of deleterious effects from sodium depletion following a limited salt intake and the abnormal loss of body fluids must be considered.

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DISCUSSION

DR. FRANK GERBODE, San Francisco.—Many of these patients who have been on a marked salt restriction diet for a long period of time have a very serious drop in serum

sodium on the second postoperative day, and it has been reported in some patients that when the sodium levels become very low, in addition to this hypotensive state which Dr. Crandell illustrated in one patient, there are also sometimes serious mental and central nervous system changes.

About one year ago, in collaboration with Dr. Quentin Deming, we embarked upon a program of giving these patients 3 Gm. of salt daily before, during, and after surgery, and in addition replacing all losses at surgery volume for volume, blood with blood, and serous fluid with saline solution; postoperative chest drainage and other nonrenal losses were replaced gram of salt for gram of salt with 0.9 per cent saline solution. No fluid other than this saline solution has been given except by mouth as the patient requested it. Since instituting this regimen we have not seen a serious fall in serum sodium concentration, and the patients appear to have been maintained in a better physiologic state. In no instance has there been pulmonary edema or precipitation of congestive failure by this treatment.

DR. GABRIEL P. SELEY, New York.—I want to congratulate Dr. Crandell on his careful analysis of these two cases, but I would like to point out that in addition to the metabolic changes it is rather risky to compare the two cases. I would like to ask him what was the situation locally; that is, how much constriction there was there, how much of the ventricles, both right and left, were involved, what the exact operative procedure was, and if he has any way of estimating what the musculature was like beneath the pericardium. I believe this information is important because certainly everyone has had the experience of doing a good resection and having a poor result, and doing a rather limited resection and having a rather good result.

DR. JOHANN L. EHRENHAFT, Iowa City.—In combination with the cardiovascular laboratory at the State University of Iowa we have studied three patients with constrictive pericarditis in an effort to demonstrate the significance of renal circulatory factors in edema formation in patients with this acquired cardiac disease. Pre- and postoperative studies were carried out. The renal plasma flow and glomerular filtration rates by standard plasma clearance methods were studied and we demonstrated a pattern of renal dysfunction identical with that of congestive myocardial decompensation. In two patients with marked hemodynamic abnormalities and massive edema, the renal dysfunction was severe. In one with mild hemodynamic aberration (associated with an interatrial septal defect) and no demonstrable edema, the renal abnormality was mild. All experienced spontaneous, diuretic weight loss in the early postoperative period. The two patients with marked weight loss of twenty-one and thirty pounds had an increase in the renal plasma flow of 84 and 80 per cent, respectively. The PAH values indicate normal tubular functional capacity in the two patients measured. Pericardiectomy was followed by modest increase in glomerular filtration rate and tremendous rise in renal plasma flow in the two patients with severe disability.

These changes probably are due to both the direct effects of restoration of hemodynamic factors toward normal, and the resultant indirect effects on neurogenic and humoral factors influencing renal water retention. Systemic venous and arterial pressure receptors may play an important role in the antidiuresis which characterizes the venous distention stage and the diuresis which occurs promptly following the postoperative increase in cardiac output and systemic arterial pressure. In the immediate postoperative period the sodium loss produced by the diuresis may be very marked, and those patients may develop signs of shock and need replacement of sodium, particularly if their reserve has been depleted by a low sodium intake in a preoperative effort to reduce edema.

DR. HARRISON BLACK, Boston.—Dr. Crandell's paper and his charts illustrate very nicely the exaggeration of electrolyte abnormalities which may become apparent postoperatively in patients undergoing cardiac operations. I believe there is one important factor, however, that has not been mentioned in this study or in the subsequent discussions, and that is the relationship between body sodium stores and the plasma sodium concentration.

At the Peter Bent Brigham Hospital we also have observed a considerable number of patients who have experienced a marked fall in serum sodium concentration after mitral valve surgery. Our lowest concentration with survival was 109 meq. per liter, and many have been found in the 120 to 125 range on the second postoperative day. The all-important factor which must be considered is the *total* amount of sodium in the body. This can be

measured by means of radioactive sodium dilution and the measurement discloses the "total exchangeable sodium." The total body water and total exchangeable potassium may also be measured and are equally important in interpretation.

Dr. Francis D. Moore and his associates, Drs. Wilson and Myrden, at this hospital, have helped us a great deal by their isotope studies in cardiac patients. As they point out, a drop in serum sodium concentration may be due to one of three mechanisms: deficiency, dilution, or "shift" into cells. We might discuss these separately.

Deficiency.—Despite the fact that many of these patients have been on a low sodium diet over long periods of time and have undergone repeated mercurial diuresis, they quite uniformly show a high total body sodium. They also show a very high total body water. Indeed, this combination of a high sodium and a high water with a low serum sodium concentration is quite characteristic of the sick cardiac patient with or without edema and either before or after surgery. It is of great interest that a low total exchangeable potassium with a relatively high plasma potassium concentration is also a part of this picture, but we are not devoting attention to that in this brief discussion. For this reason, we have felt that true sodium deficiency is rarely a part of this picture and, indeed, it does not seem logical to treat the patients pre- or postoperatively with concentrated salt solution except under most exceptional circumstances.

Dilution.—The studies have shown in addition that cardiac patients when allowed unrestricted oral intake after surgery are extremely prone to gain body water. This is manifested clinically by gain in weight. It is apparent that even though no salt is given, these patients are still able to accumulate excessive body water and this, of course, may contribute further to the lowered serum sodium concentration. It is of importance to note that during hot summer weather when skin and lung losses are higher, this tendency is not so apparent.

"Shift."—Although great care may be exerted to avoid extra water loading in these patients, they will still show some drop in serum sodium concentration. Dr. Moore's group some years ago demonstrated that trauma itself tends to produce a lowering of the serum sodium concentration in the presence of a positive sodium balance, and they have felt that this is due to translocation or "shift" of sodium into cells. There is recent evidence that in cardiac patients this tendency may be especially marked. It should be emphasized also that intracellular water, newly appearing in the extracellular phase, might contribute to this appearance of "shift."

Before these studies were available to us, we too gave our postoperative cardiac patients hypertonic sodium chloride when a low serum sodium value was associated with the clinical features of the "low sodium syndrome" (that is, hypotension, apathy, and disorientation). We were impressed with the fact that on many occasions this therapy was coincident with a rapid correction of the clinical aberrations and a rise in the serum sodium level. However, I am equally sure that in a few cases the salt load aggravated congestive failure with lethal outcome in at least one instance.

Taking all these factors into consideration we have modified our routine by restricting patients to 1,500 c.c. of fluid (oral plus parenteral), in the first twenty-four hours, not including in this the blood replacement. On the second and third days the same amount is allowed and the ration is not increased until the usual spontaneous diuresis occurs. In hot weather this figure will probably have to be increased. With this method of management we have found that very few patients experience the severe drop of serum sodium concentration that we formerly saw, and the dangerous clinical features of the syndrome have become a thing of the past. The result is that we have not found it necessary recently to use hypertonic salt solution. Therefore, on the basis of these total balance studies, I believe we may conclude that the administration of saline solution to cardiac patients either preoperatively or postoperatively in the vast majority of instances is not rational and, in fact, may be dangerous.

DR. K. ALVIN MERENDINO, Seattle.—The points which Dr. Crandell brings out are certainly of great significance and I arise, as did Dr. Black and Dr. Gerbode, to broaden the implications of the points which have been made. Following mitral commissurotomy, we unwittingly ran into a patient on the second postoperative day with hallucinations and apprehension. The serum sodium was 118 meq. and the chloride 69 meq. This led us to

attempt to uncover the symptoms that would lead us to suspect this condition in other patients. Therefore my colleagues, Drs. Robert Bruce, Marcelle Dunning, Belding Scribner, and I followed ten consecutive mitral commissurotomy patients with balance studies. No electrolyte of any kind was given during the postoperative period. However, the patients were allowed to take by mouth a formula of known composition. A negligible quantity usually was taken for the first three days. This gradually was increased.

(Slide.) This shows the life history of this syndrome without any therapy whatsoever. These graphs represent the daily balance studies on these patients. The minimal, maximal, and mean responses are recorded. The serum sodium levels fell within the first two days postoperatively from an average of 142 meq. to an average of 126 meq. Serum potassium revealed a slight rise; the chlorides fell to their lowest level the third day, a lag of twenty-four hours behind the sodium fall for some unknown reason. Electrolyte studies on the urine revealed a renal conservation of sodium as well as potassium during the same period. This was probably related to a low intake. The chloride changes were not significant.

(Slide.) During the initial two- or three-day postoperative period, there is a positive water balance. The recorded output includes not only urinary output but a rough approximation of insensible loss. As you can see there is a positive water balance in extreme cases up to 2 L. but on the average it is 850 c.c.

(Slide.) We have been able to catalog the severity of the patients' symptoms on the basis of the serum sodium levels. Seven of these eleven patients had symptoms. Those with moderate symptoms had sodium levels of 120 to 130 meq. Those with severe symptoms had sodium levels of 111 to 120 meq. As long as the serum sodium remained about 120 meq. the symptoms were not severe.

(Slide.) These are the symptoms encountered in this group of patients. In the moderate group, asthenia, lethargy, anorexia, and variable sweating were observed. The severe group had cerebral disturbances which included apprehension, hallucinations, and delirium, even to the point of coma.

(Slide.) In our opinion these are the contributing factors, some of which have been mentioned by Dr. Crandell and the other discussers, namely, preoperative salt depletion, salt deprivation postoperatively, the administration of a nonelectrolyte containing fluid, nonspecific stress responses, and pleural drainage which contains on an average of 66 meq. for the first one to four days postoperatively but may be as high as 160 meq. It appears that no single factor is sufficient to produce the hyponatremic levels observed. All factors are participating in a greater or lesser degree in each individual patient, as well as other factors incompletely understood at present.

(Slide.) In the next fourteen consecutive mitral commissurotomies we conducted a prophylactic program. All patients on the day of surgery and daily thereafter were given 73 meq. of sodium (500 c.c. saline solution). This was supplemented with additional saline as indicated by the serum sodium levels. Some patients have received as much as 20 Gm. of sodium chloride in one day. No attempt was made, however, to restore the serum sodium to normal levels in the early postoperative period. From the practical point of view, other things being equal, the serum sodium level is the most important single laboratory procedure in the management of cardiac patients following surgery. In this fashion, we have been able to prevent the extreme degrees of hyponatremia and the severe symptoms and signs associated with it.

DR. CRANDELL (Closing).—Time would not permit answering Dr. Seley's questions. I will try to answer them indirectly in this fashion. You will recall that the young man, aged 27 years, had a poor immediate postoperative response and the older man, aged 54 years, had a good response. Although the young man immediately entered a stormy period, he has ultimately had an excellent result, to the extent that two years after the pericardial resection he was able to carry a 150-pound deer two miles out of the woods without any trouble. On the other hand, the older man has experienced a considerable limitation of activity.

I am very grateful to Dr. Gerbode for his discussion, and to Dr. Black, who has helped provide answers to questions about which we are curious. I certainly envy his facilities in having available radiosodium and deuterium oxide. I wish to thank Dr. Merendino for his discussion.

BRONCHIAL CLOSURE IN PULMONARY RESECTION: A CLINICAL AND EXPERIMENTAL STUDY USING A PEDICLED PERICARDIAL FAT GRAFT REINFORCEMENT

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INTRODUCTION

PERMANENT bronchial closure is the basis of a successful pulmonary resection. Current methods are generally quite effectual when the bronchus is normal, although a wide variation in results is reported. However, when the bronchial wall is diseased and friable and the stitches fail to hold, surgeons agree that there is an urgent need for an occlusive reinforcing tissue. A highly effectual method of developing a viable, pedicled pericardial fat graft reinforcement to the bronchial stump was devised by one of us (L. A. B.) in July, 1949, after trying pleura and other tissues. Our technique of closing the bronchus and of developing the graft is presented, along with pertinent data concerning clinical and experimental observation. A review of 323 cases of total pneumonectomy and lobectomy for malignant and nonmalignant disease is made. The superiority of this method, in our experience, is shown by comparing the results with this technique in 221 cases, to those of an earlier series of 102 cases in which the "thoracic omentum" was not used.

HISTORICAL DATA

With the risk of oversimplification, we have divided the history of pulmonary resection and bronchial closure into four definite periods, in order to condense an extensive review.

1. Period of "fortuitous" pulmonary resection (1496 to 1880, and even later).
2. Period of animal experimentation (1880 to 1900).
3. Beginning modern period (1890 to 1928).
4. Present-day period (1929 to the present time).

1. Period of "Fortuitous" Pulmonary Resection.—Before the understanding of pulmonary and intrathoracic physiology had been developed (latter part of nineteenth, and early twentieth centuries), a few intrepid surgeons were successful in excising relatively small amounts of peripheral pulmonary tissue, aided by the fortuitous fusion of the pleura and a fixed mediastinum. Since these early successes in the removal of pulmonary tissue have almost completely escaped notice in the medical literature, we are including a brief description of the three earliest pulmonary resections that we have been able to discover.

The first recorded excision of lung tissue was reported by an Italian, Rolando of Parma,[1] in 1496. He was called to treat a man of Bologna who had

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suffered a severe wound of the thorax, in which the lung was protruding on the chest wall. The patient had been given up by other surgeons, and on the sixth day after the wounding, the lung presented as a mortified, gangrenous tissue. Rolando excised this lung tissue, and to his amazement the wound healed, aided no doubt by the beneficial débridement of maggots. Since this excision of lung tissue was in complete violation of all the surgical precepts of the age, Rolando was happy to report that the man was perfectly well one year later and able to make a trip with his master to Jerusalem.

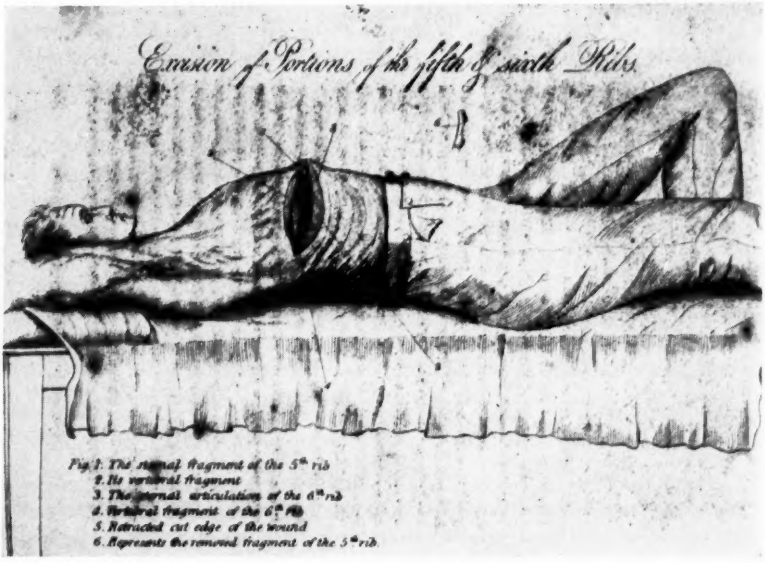

Excision of Portions of the fifth & sixth Ribs
Fig. 1. The sternal fragment of the 5th rib
2. Its vertebral fragment
3. The sternal articulation of the 6th rib
4. Vertebral fragment of the 6th rib
5. Retracted cut edge of the wound
6. Represents the removed fragment of the 5th rib

Fig. 1.—Drawing of the thoracotomy incision reported by Milton Anthony of Augusta, Ga., in 1821. Published in *The Philadelphia Journal of the Medical Sciences* in 1823.

This surgical feat was unknown for centuries, and it remained for an American pioneer, Milton Anthony,[2] in Augusta, Ga., to record the first deliberate entrance of the pleural cavity in 1821 and the removal of "one to two pounds" of pulmonary tissue, along with the portions of two ribs. The man he treated had a swelling in the thorax which came on approximately one year after an injury to the chest. The tumor of the chest wall was incised and sections of the fifth and sixth ribs were excised, along with portions of necrotic lung tissue. The exact nature of the pathology was not known although it could have been a neoplasm of the chest wall and lung or some sort of chronic inflammatory process. However, after the thorax had been opened, to Anthony's "utter astonishment and mortification," he was able to palpate "more or less disorganized fragments of bronchial tubes." He then guided the hand of his intrepid assistant, Dr. Pugsley, "an aged, experienced and accurate surgeon and anatomist" into the chest to feel the extensive destruction of the right lung. Anthony, a compassionate man, did not wish to discuss out loud

this shocking finding, in order not to "alarm" his conscious, but stoical patient. The man recovered from the surgery to succumb at a distant hamlet one year later. Fig. 1 is a reproduction of the incision used by Anthony in his published report in 1823.

In 1861, Jules Emile Pean,[3] a Parisian, apparently with the benefit of general anesthesia, excised a pulmonary tumor and portion of the lung. The patient had a small tumor at the level of the fourth intercostal space, which caused him severe and intolerable pain. After aspiration of the tumor yielded no fluid, an exploratory incision was made. To Pean's surprise a tumor arising in the lung adherent to the pleura was found. The tumor was drawn out, after having effected adherence of the parietal and visceral pleura at a number of points by interrupted sutures. The tumor was then excised by galvanocautery. Hemostasis was further effected by leaving on several hemostats and by "Phoenician" dressing. The patient was apparently cured by this operation and was reported in good health one year thereafter. Since Pean had the insight to sew the two layers of the pleura together, this case was not as "fortuitous" as the others. However, from the point of view of bronchial closure, only peripheral lung tissue was excised and no bronchus of moment was divided. Thus, bronchial closure had not yet become a problem in pulmonary resection.

2. Period of Animal Experimentation (1880 to 1900).—Because of the general use of anesthesia and the discovery of microorganisms and antiseptics, many techniques for abdominal operations were perfected during the latter quarter of the nineteenth century. Faced with the disasters in opening the thorax of human beings, a few surgeons, notably German, turned to the experimental laboratory to study suitable methods of lung excision. The Germans, Gluck,[4] Schmid,[5] Block[6]; the Italian, Biondi[7]; the Englishman, Willard[8]; the Americans, LeMoyne Wills[9] of Los Angeles, and Murphy[10] of Chicago performed pulmonary resections on experimental animals. Murphy made the important observation that if the mediastinum was fixed, the pleural cavity could be opened without severe anoxia, but if the mediastinum was mobile, anoxia and death resulted. These experiments shed light upon the problems of open pneumothorax and mediastinal shift and resulted in the cautious, but realistic attitude of the clinical surgeons. They showed, moreover, that lobes and lungs could be resected but that a high mortality resulted. Mass ligation of the structures at the hilum was the technique that ushered in the early modern period of pulmonary resection. Bronchial fistulas were almost invariably present in the animals surviving the operative shock and sepsis. Bronchopleural fistula was recognized as a hazardous and almost inevitable complication of pulmonary resection.

3. Beginning Modern Period (1890 to 1928).—Stimulated by experimentation, Tuffier,[11] in 1891, resected the apex of the lung affected by localized tuberculous disease. He used an extrapleural approach and closed the wound

without drainage. The patient made an uneventful recovery and was well and working four years after the operation. In 1901, Heidenhain[12] performed a successful lobectomy for bronchiectasis.

The problem of open pneumothorax continued to vex the surgeon despite the experimental work of the preceding period. Sauerbruch,[13] in 1904, introduced his "reduced pressure operating cabinet" which sought to obviate this difficulty. The patient and the surgeon were placed in a roomlike cabinet in which the pressure was reduced by 18 to 20 mm. of mercury. The patient's neck and head extended out of the cabinet. An airtight seal was made about the neck. Thus, the patient could breathe in room air and the collapse of the lung was counteracted by the negative pressure. In 1908, in this country, Willy Meyer[14] perfected a positive pressure cabinet. This cabinet was placed about the head of the patient and was large enough to accommodate the anesthetist. Positive pressure in the cabinet from 20 to 25 mm. of mercury protected the lung from collapse when the thorax was open.

During the first decade of the twentieth century, work on endotracheal anesthesia continued. Following the efforts of Tuffier, Matas[15] and others, Elsberg[16] reported endotracheal insufflation anesthesia with a positive pressure of 20 mm. of mercury. This technique was further developed and popularized by McGill[17] in the 1920's. And endotracheal anesthesia became the standard form of anesthesia for intrathoracic operations. It was used by Lillienthal[18] in the majority of the twenty-two lobectomies with a 42 per cent mortality that he reported in 1922. However, he regarded the positive pressure chamber as being useful in cases "in which it was desirable to keep the thoracic wound open for a few hours or even days after the operation." The high mortality with lobectomy stimulated Graham[19] to develop the procedure of cautery pneumonectomy, which he reported in 1923. The actual destruction of the bronchiectatic lung tissue by the cautery method resulted in a relief of the patient's symptoms, with a lessened mortality. In reviewing the advances of this period, we are impressed by the fact that it was now possible to open the thorax and remove lung tissue, even entire lobes of the lungs, aided by endotracheal anesthesia. The bronchial stump in pulmonary lobectomy was still controlled by mass hilar ligation. Bronchial fistulas were the expected complications of lobectomy, as an anatomic approach to the closure of the bronchus had not yet been perfected, and successful pneumonectomy in human beings was still an unsolved problem.

4. Present-Day Period (1928 to Present Time).—Brunn,[20] in 1929, reported the technique for one-stage lobectomy which may be regarded as ushering in the present-day period of pulmonary resection. He presented six cases in which lobectomy was performed with one operative death. The pedicle of the lobe was clamped and double, interlocking chromic catgut sutures were tied to control the vessels and the bronchus. The pedicle was then closed over with a running stitch of chromic catgut.

In 1932, Shenstone and Janes[21] reported the technique of tourniquet lobectomy. The use of a tourniquet made the operation considerably safer and

the size of the lobar stump was smaller. This technique was quite generally accepted until the beginning of World War II. In 1931, Nissen[22] performed a two-stage pneumonectomy for bronchiectasis with mass ligation of the hilum. The lung was allowed to slough off. In 1932, Haight[23] also reported a successful two-stage pneumonectomy. The year 1933 will be remembered for the first successful one-stage pneumonectomy for carcinoma, performed by Graham.[24] Resection of the lung by one-stage procedure had now become feasible and new impetus was given to pulmonary resection.

Shortly after this, Rienhoff[25] introduced a method of individual ligation technique for the hilar structures in pneumonectomy. The technique, with some modifications, is in use today. In 1939, Churchill and Belsey[26] reported the individual ligation of the lobar and segmental vessels and bronchus with segmental pneumonectomy of the lingular segments of the left upper lobe for bronchiectasis. Kent and Blades,[27] in 1942, reported the sound anatomic approach to pulmonary resection by the individual ligation of the vessels and bronchus for the respective lobes of the lung. At last precise surgical technique had been developed and no longer were bronchial fistulas accepted as the inevitable complications of lobectomy or pneumonectomy.

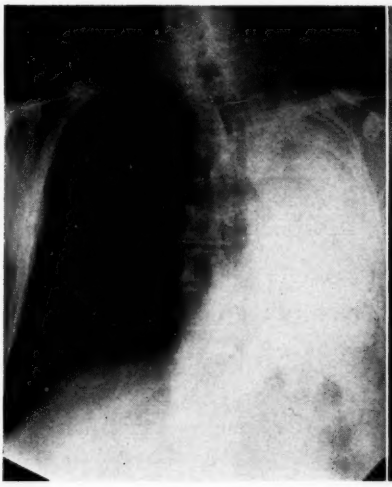


Fig. 2.

Fig. 3.

Fig. 2 (Case 1).—Preoperative chest x-ray film shows total atelectasis of the left lung, which was caused by an adenoma obstructing the left main bronchus.

Fig. 3 (Case 1).—X-ray view of chest, one year following total pneumonectomy. The severed bronchus leaked air following pneumonectomy. It was successfully closed with a pedicled pericardial fat graft.

AUTHORS' MATERIAL

Our technique of employing pericardial fat graft to reinforce the bronchial stump was born out of sheer desperation in a case where we were unable to close securely a diseased bronchus. Fig. 2, the preoperative film of this case, shows a benign adenoma of the left main bronchus which had produced

total atelectasis of the left lung. The patient had had a chronic cough for years, and there was considerable bronchitis in the portion of the bronchus above the tumor, in the vicinity of the carina. On July 1, 1949, while resecting the left lung which had been destroyed by the protracted bronchial obstruction, great difficulty was encountered by one of us (L. A. B.) in effecting closure of the diseased bronchial wall at the carina. However, an airtight suture of the bronchus was effected and the chest wall was closed. Immediately following the operation, on hard coughing, it was obvious that the bronchus had re-opened. The chest was again entered and the torn bronchus noted. Further attempts to close this tear resulted in extension of the rent up into the tracheal wall. Borrowing from the experience in surgery of the abdomen, where omentum has been successfully used for years to seal off the repair of a ruptured peptic ulcer, it was decided that a pedicled pericardial fat graft, in a similar manner, might seal off the aperture in the bronchial and tracheal walls. Such a graft was fashioned and sutured to the incompletely closed bronchial stump and trachea. The closure remained airtight, and the patient made an uneventful recovery. Fig. 3 shows the film one year following surgery.

Following this gratifying result we decided to investigate this technique further on experimental animals.

EXPERIMENTAL OBSERVATIONS

In a series of twenty-one mongrel dogs, pedicled pericardial fat grafts were developed for bronchial reinforcement in either total pneumonectomy or lobectomy. To simulate the conditions of our original case, the bronchial stump was incompletely closed so that there was a definite blowing of air on application of positive pressure to the bronchial stump following the pulmonary resection. A pedicled, pericardial fat graft was then developed, usually from the middle portion of the mediastinum and firmly fixed to the bronchial stump, according to the technique to be described for human beings later in this communication.

We experienced some difficulty in developing these grafts for two reasons: First, the pericardial adipose tissue was extremely thin and friable and did not exhibit as satisfactory a blood supply as that found in human beings, and great care had to be exercised in developing the grafts so as not to tear the very fragile mediastinal pleural septum and enter the opposite pleural space. That this septum exists as an effective barrier between the pleural spaces is much disputed; however, our experience along with that of many others points to the presence of this septum as a fragile but definite barrier between the two pleural cavities. We are pleased to note that *the grafts effectively closed the bronchi and prevented the dogs from developing bronchial fistulas and empyema in all instances.* It should be emphasized, however, that these dogs were all given penicillin for three or four days following operation. It is also true that the bronchi were apparently grossly normal in all instances. In our experience, lobectomy and pneumonectomy in dogs protected by antibiotics, with or without the grafts, have a very low rate of bronchial fistula.

The cartilage of the dog's bronchus is so flexible that it is not necessary to make an elliptical flap of the membranous portion of the bronchus, as we routinely do for major bronchi in human beings. After performing five pneumonectomies, we performed lobectomies on subsequent animals as it was apparent that we could study the viability and fate of the graft just as well. Furthermore, following the lobectomy, the animal was available for other intrathoracic procedures (most of them cardiovascular), which were performed on the same and, in some instances, on the opposite side of the chest.

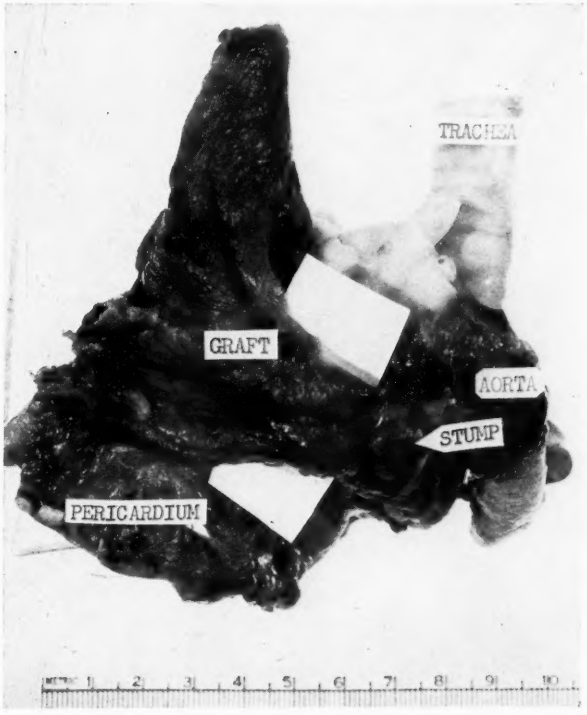


Fig. 4.—Dog 3-D. Gross specimen of pedicled pericardial fat graft covering bronchial stump three days after left total pneumonectomy had been performed. Specimen shows the pedicled graft firmly in place, tightly reinforcing the bronchial stump.

In all cases, when observed at autopsy, or at subsequent operations, the grafts were intact and appeared to be grossly viable and firmly fixed to the bronchial stump. The maximum period of observation was one year.

Microscopic studies were made upon the grafts from periods of twenty-four hours up to one year. The suture material had to be picked out of the blocks before they were cut and this practically always frayed the sections. In twenty-four hours, the graft was adherent to the bronchus, the fat cells were intact, and a leukocyte infiltration was present. By three days (Figs. 4, 5, and 6) the leukocyte infiltration had increased, some edema fluid was

present, and fibroblastic proliferation was noted, uniting the bronchus and fat graft. By the eighth day (Figs. 7, 8, 9, and 10) fibroblasts had increased in the zone of tissue that marks the junction of the pericardial fat graft and the cut ends of the bronchus. Columnar epithelium had bridged over the fat graft.

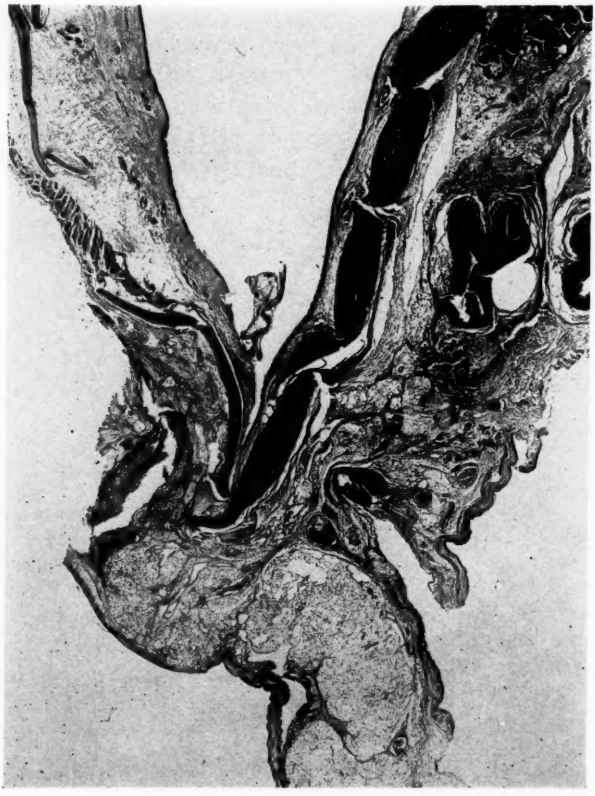


Fig. 5.—Dog 3-D. Low-power view of sagittal section of bronchial stump three days after left total pneumonectomy. The pedicled pericardial fat graft appears in the lower center of the field, covering the incompletely closed bronchial stump. Although the section is torn, the beginning fibrous union of fat graft and bronchus can be seen.

Further out in the fat graft, irregular areas of fibroblastic proliferation and all the early signs of organization were present. Macrophages with hemosiderin represented the phagocytosis of hemoglobin from operative hemorrhage. After one month's time or more, adult type of fibrous tissue was present in the part of the fat graft next to the bronchus with irregular involvement of more peripheral portions of the graft. In four months' time (Fig. 11) the fibrosis was perhaps a little more advanced, otherwise there was very little change up to one year's time. No further fibrosis of the fat graft was noted after this. Intact fat cells were present and the vascularity of the graft was evidenced by the finding of small blood vessels in all sections.

Our findings are similar in some ways to the experimental observations on dogs made by Rienhoff.[28] He reported that there was a marked tendency in dogs to bridge over defects in bronchial closure by proliferation of submucosal and peribronchial tissue, together with granulation tissue derived from the nonserous surface of a mediastinal pleural graft. In our experiments, the viable pericardial fat graft was used in place of pleura. We did not notice the great tendency for the bronchial walls to separate at the site of closure that he reported. Perhaps, the pericardial fat graft helped to hold the bronchus together. The microscopic study of the bronchial stumps, reinforced with the pericardial fat grafts, confirmed the gross observations of the effectiveness of these grafts as a bronchial reinforcement. The grafts are truly linked to the bronchial stump by a fibrous union.

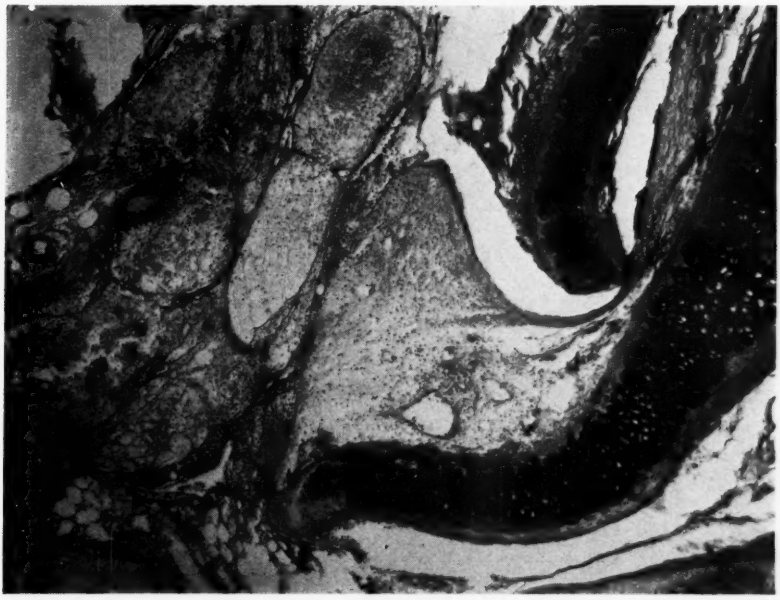
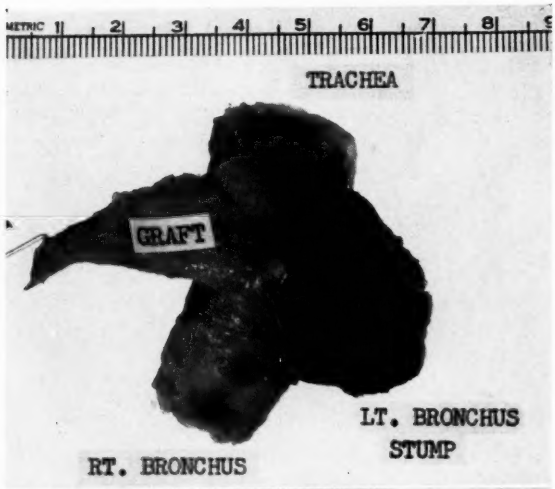


Fig. 6.—Dog 3-D. High-power view of sagittal section of bronchial stump seen in Fig. 5. Viable adipose tissue blocks the opening between the two cartilages. Early fibroblastic proliferation has begun. Epithelium has not regenerated.

TECHNIQUE OF BRONCHIAL CLOSURE

In closing the main bronchus we used a simple interrupted suture, bringing the soft membranous portion of the bronchus to the fixed cartilaginous wall. To effect this closure without tension, a slightly oval-shaped flap is cut from the posterior membranous portion of the bronchus, so that it would meet the more rigid cartilaginous wall. No clamps are placed on the bronchus at the site of suture and an "open" type of closure is used. The bronchial arteries are carefully preserved. With lobar bronchi, the closure is more easily

Fig. 7.



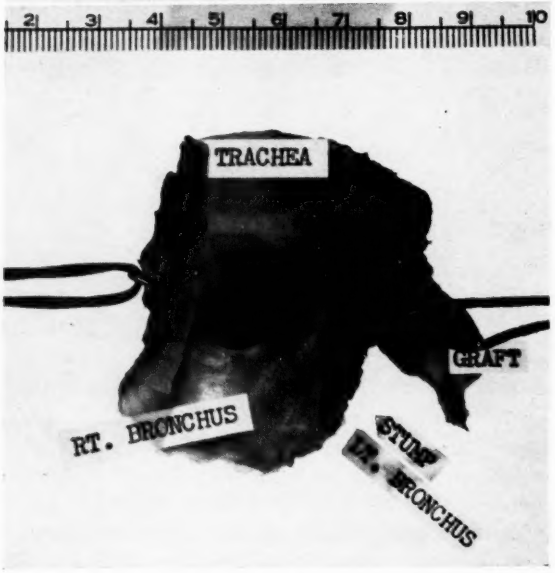


Fig. 8.

Fig. 7.—Dog 165. Gross specimen of left bronchial stump eight days after total pneumonectomy. Graft firmly adherent to the bronchial stump.

Fig. 8.—Dog 165. Gross specimen of inside of left bronchial stump eight days after pneumonectomy. Complete epithelization of incompletely closed bronchus is seen.

Fig. 9.

Fig. 10.

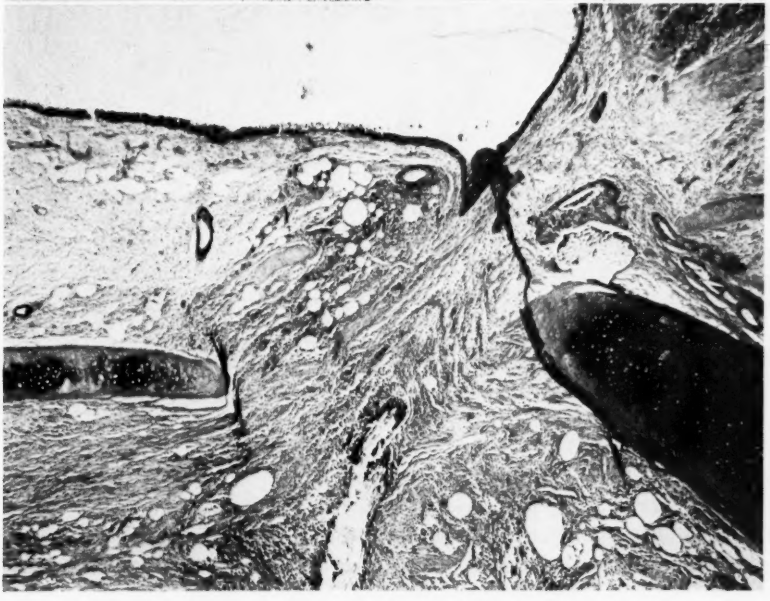


Fig. 9.—Dog 165. Low-power view of sagittal section of bronchial stump eight days after pneumonectomy shown in Figs. 7 and 8. Fat graft occupies lower portion of section. Fibrous union with bronchial wall is seen.

Fig. 10.—Dog 165. Medium-power view of sagittal section of bronchial stump. Fat graft fills in aperture between two cartilages. Fibrous tissue and cellular infiltration are present. Epithelium has bridged the gap in the mucosa.

effected, since the cartilage is softer and the walls usually collapse without tension on a simple right-angled division of the bronchial wall. The formation of the cartilage may be irregular and completely surround the bronchus, leaving no posterior membranous wall. However, in many instances the anatomy of the lobar bronchus resembles that of the main bronchus.

Fig. 11.—Dog 121. Medium-power view of microscopic section of bronchial stump four months after lobectomy. Fat graft is shown to be viable, and fixed to bronchial wall by adult connective tissue which is also present deeper in the graft. Note the blood vessels in the graft.

The exact technique of the bronchial closure of a main bronchus is shown in Fig. 12. For suture material, we have used tantalum wire, 0.007 inch in diameter onto which a fine needle has been tightly swedged. The diameter of the needle is approximately the same as that of the wire, and thus it does not make a hole in the bronchial wall that may eventually leak. Care is taken to cut the cartilaginous wall along the upper edge of the cartilage, leaving 1 to 2 mm. of membranous wall behind, if possible, which is more suitable for the bronchial closure. The wire sutures are tied just tightly enough to approximate the walls of the bronchi so that there is no leakage. If the wire sutures are tied too tightly they will cut through the bronchus. The cut ends of the wire are turned in so as not to sever any of the major vessels of the hilum. The graft offers further protection to the wire ends. However, on upper lobe branch bronchi we have routinely used fine arterial silk, fearing erosion of the pulmonary artery from the ends of the wires may otherwise result.

DEVELOPMENT OF VIABLE PERICARDIAL FAT GRAFT

The anatomy of the mediastinum and the pericardial fat is depicted on the diagram (Fig. 13). The fatty tissue in the pericardium and the anterior mediastinum receives its blood supply mainly from branches of the internal mammary artery. However, branches of the pericardiophrenic and musculophrenic arteries also send nutrient branches to this fatty tissue. The pericardiophrenic artery accompanies the phrenic nerve between the pleura and the pericardium to the diaphragm, where it anastomoses with the musculophrenic and inferior phrenic arteries. The anterior mediastinal branches of the internal mammary artery supply the areolar and adipose tissue in the anterior mediastinum, along with the remains of the thymus. The main pericardial branches of the internal mammary artery are two in number: a superior branch to the superior

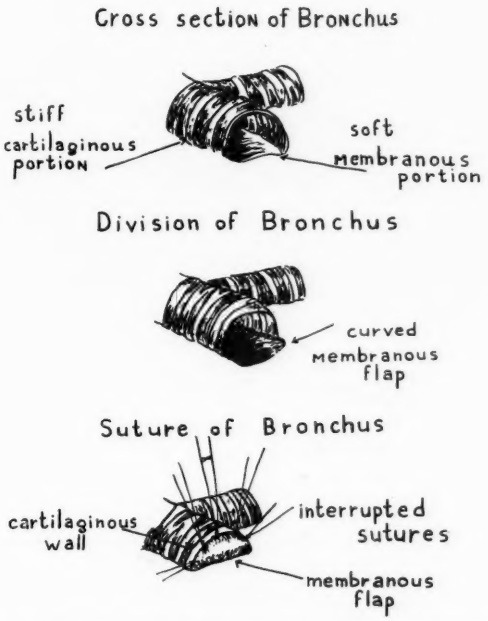


Fig. 12.—Technique of closure of the bronchus used by us.

pericardium, and a middle branch to the midportion of the pericardium. This middle branch is a fairly large and constant vessel and is the one that supplies the blood to the graft in the great majority of instances. The inferior pericardial branch comes from the musculophrenic branch of the internal mammary artery.

The anterior mediastinal, pericardial, and sternal branches, together with some twigs from the pericardial phrenic artery, anastomose with branches from the intercostal and bronchial arteries to form the subpleural mediastinal plexus.[29] The veins draining this plexus are less uniform in their course than

are the arteries, but they tend to follow the arteries. It is from the branches of this plexus, some of which may not be readily visible to the naked eye, that the blood supply of the pericardial fat graft is maintained, even though a fairly long pedicle is developed. There may be considerable variation in the course of the branches of the internal mammary arteries that supply the adipose tissue; however, with a careful inspection of these branches the graft may be so planned as to include a satisfactory blood supply in over 95 per cent of the cases.

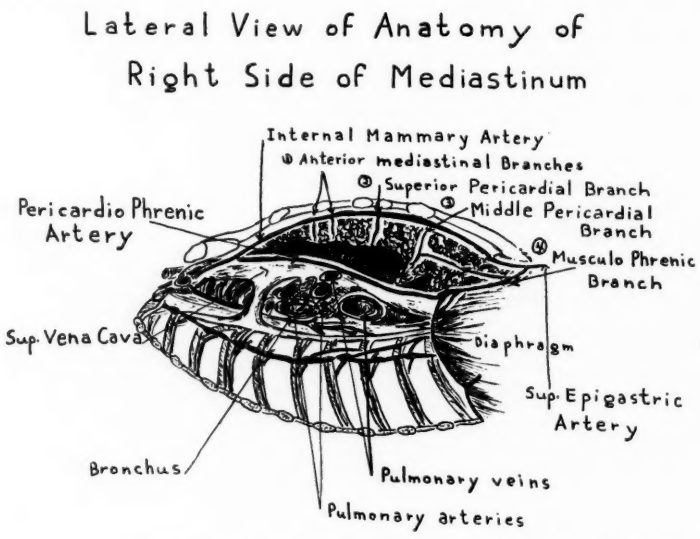


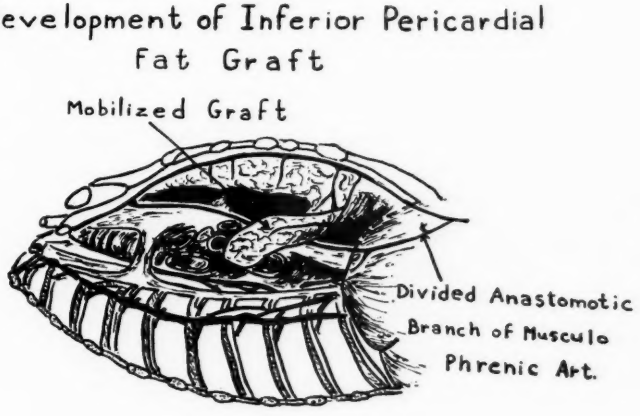
Fig. 13.—Diagram of anatomy of right side of mediastinum, showing the blood supply to the pericardial and mediastinal adipose tissue.

We have found that the most satisfactory pericardial fat graft can be developed from the anterior inferior mediastinum, utilizing the adipose tissue that lies directly over the diaphragm. The blood supply to this portion of the pericardial fat comes from the musculophrenic artery, the middle pericardial branch of the internal mammary artery, and a few twigs from the pericardiophrenic vessels. There is a fairly constant branch that connects the middle pericardial branch of the internal mammary artery and the musculophrenic artery which, when present, provides an excellent blood supply to the mobilized graft, after the division of the branches of the musculophrenic and pericardiophrenic arteries. Because the pericardial fat extends for a distance anteriorly to cover the anterior surface of the heart, satisfactory lengths of the graft may be obtained. The blood supply is entirely from the vessels mentioned, and there are no vessels of any moment running down the mediastinum mesial to the internal mammary artery. In the case of a middle or lower lobe lobectomy, no difficulty at all is encountered in obtaining satisfactory length of the graft. However, in an upper lobe lobectomy, or pneumonectomy, con-

siderable care must be exercised in preserving the blood supply to obtain a satisfactorily viable graft. The freeing up of the graft is shown in Fig. 14. In some instances it may be necessary to divide the internal mammary artery below the junction of the middle pericardial branch, ligate the perforating intercostal and sternal branches, and dissect the internal mammary artery upward so as to obtain additional length of graft with adequate blood supply. However, with a little care and practice, the graft is readily developed.

Four sutures are then placed at equal intervals on the circumference of the bronchial stump. With the tip of the graft turned back, the mesial and

Fig. 14.



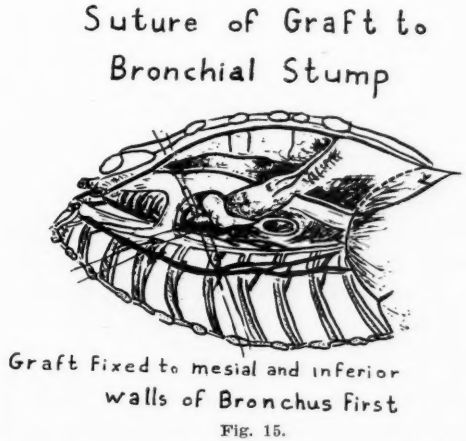


Fig. 15.

Fig. 14.—The inferior pericardial fat graft is developed by dividing anastomotic branch of musculophrenic artery and the pericardiophrenic branches.

Fig. 15.—Graft sutured to bronchial stump by interrupted sutures.

inferior sutures are sewn to the graft and tied first (Fig. 15). Then, the superior and lateral sutures are affixed to the graft so that it fits over the stump of the bronchus, like a cap. Additional interrupted sutures of fine silk are now placed in the tissue about the bronchus to fix the graft firmly in place and make the reinforcement airtight (Fig. 16). The graft is further firmly sutured to the mediastinum and pericardium to take the tension off the bronchial stump on coughing and invite early union of the graft to these structures.

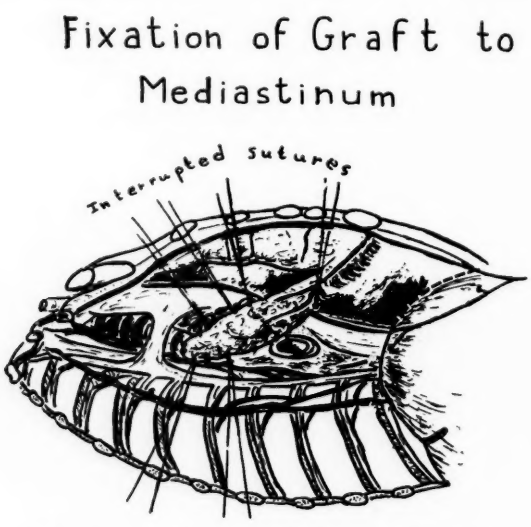


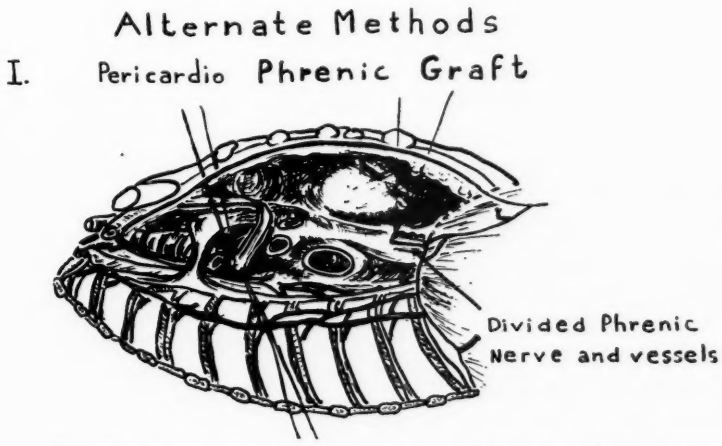
Fig. 16.—Graft is firmly fixed to the mediastinum.

Two alternate methods of developing a fat graft are available at times when the one described is not feasible. There is always a certain amount of adipose tissue that accompanies the phrenic nerve and the pericardiophrenic vessels. If it is desirable to sacrifice the phrenic nerve, then the nerve and the pericardiophrenic vessels and adipose tissue may be divided just above the diaphragm, and these structures are carefully teased off the pericardium and developed as a graft which is fixed to the bronchial stump in the previously described manner (Fig. 17).

In some instances, the scantiness of free adipose tissue accompanying the nerve and vessels makes this graft unsatisfactory. Another form of anterior mediastinal fat tissue graft, though not strictly pericardial, may be developed from the adipose tissue in the anterior superior mediastinum where the blood supply comes mainly from the anterior mediastinal vessels and the superior pericardial branches of the internal mammary artery. Here the blood supply is not usually as good as that of the inferior pericardium; however, a shorter pediele needs to be developed as the distance from the anterior superior mediastinum to the main-stem bronchus or the upper lobe bronchus is less than that

from the inferior mediastinum. We have used this type of graft in a small number of cases. The technique of application is shown on Fig. 18. It should be added that in the case of the inferior pericardial fat graft in which the middle pericardial branch of the internal mammary is used for the blood supply, the graft serves to form a sling reinforcement to the heart when the pericardium has been resected for an intrapericardial ligation of the pulmonary vessels in the case of a hilar carcinoma. Sometimes it is possible to fix the graft to the edges of the opened pericardium and thus prevent herniation of the heart, which, unless it is immediately relieved, is usually a fatal complication.

Fig. 17.



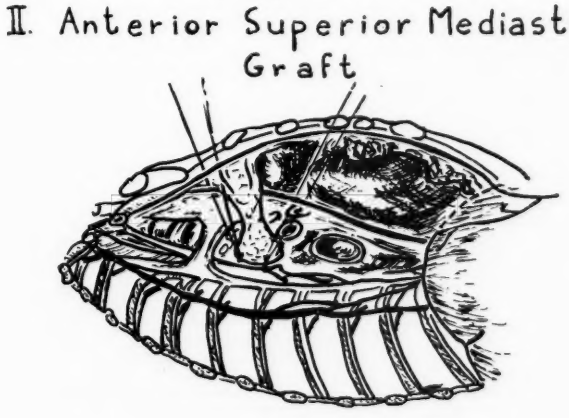


Fig. 18.

Fig. 17.—Adipose tissue accompanying the phrenic nerve is supplied by the pericardiophrenic vessels. When phrenic nerve can be sacrificed, this provides an alternate method of bronchial stump reinforcement.

Fig. 18.—Anterior mediastinal branches of the internal mammary artery supply adipose tissue in anterior mediastinum suitable for bronchial stump reinforcement.

TABLE I. TOTAL PNEUMONECTOMY AND LOBECTOMY IN PERICARDIAL FAT GRAFT SERIES (JULY, 1949, TO FEBRUARY, 1953)
221 CASES

	PNEUMONECTOMY	LOBECTOMY
Carcinoma	89	9
Pulmonary tuberculosis	20	32
Bronchiectasis	9	40
Lung abscess	0	21
Bronchial adenoma	0	1
Total	118	103

CLINICAL RESULTS

In all, 323 cases of either total pneumonectomy or lobectomy were reviewed to determine the effectiveness of the bronchial closure and the pericardial fat graft. In 221 cases, the technique outlined with the pericardial fat graft reinforcement was employed (Table I). While in 102 cases no pericardial fat graft was used (Table II). We believe these two series are very comparable because all the operations were performed by one of us (L. A. B.) with the exception of a few cases, so that the technique was the same in the two series, except for the application of the fat graft in one instance and the use of some other form of reinforcement in the other.

TABLE II. TOTAL PNEUMONECTOMY AND LOBECTOMY IN PREPERICARDIAL FAT GRAFT SERIES (JULY, 1946, TO JUNE, 1949)
102 CASES

	PNEUMONECTOMY	LOBECTOMY
Carcinoma	26	8
Pulmonary tuberculosis	8	3
Bronchiectasis	5	26
Lung abscess	3	14
Bronchial adenoma	4	5
Total	46	56

The results of these techniques are compared on Table III. It will be noted that the incidence of bronchial fistula in the prefat graft series was 7.9 per cent, almost one-half of these occurring in the first two weeks; while in the larger series of cases in which the fat graft was employed, there were no bronchial fistulas occurring in the early, critical first three weeks. In this series a late occurrence of bronchial fistulas, up to five months after operation, was 2.5 per cent. It is further noted that bronchial fistula was the main cause of death in three of the earlier cases (Table IV). Thus, it is apparent that

TABLE III. COMPARISON OF RESULTS PRE- AND POSTPERICARDIAL FAT GRAFT REINFORCEMENT. INCIDENCE OF BRONCHIAL FISTULA

	WITHOUT GRAFTS (102 CASES)		WITH GRAFTS (221 CASES)	
	Early First 3 weeks	Late Fourth week plus	Early First 3 weeks	Late Fourth week to fifth month
Pneumonectomy	5	1	0	5
Lobectomy	0	2	0	1
Total	5 +	3 = 8 (7.9%)	0	6 = (2.7%)

TABLE IV. ANALYSIS: BRONCHIAL FISTULA (PREGRAFT SERIES)

	AGE	SEX	DIAGNOSIS	FISTULA	PATHOLOGY OF BRONCHUS	REINFORCEMENT	CAUSE DEATH
				Pneumonectomy (46 Cases)			
1	35	F	Pulmonary tuberculosis	2 days	Tuberculous bronchitis	Pleura	Yes
2	69	M	Carcinoma	8 days	Chronic bronchitis	Gelfoam	Yes
3	32	F	Hodgkins disease	10 days	Radiation bronchitis	Pleura	No
4	58	M	Pulmonary tuberculosis	13 days	Tuberculous bronchitis	Areolar tissue	Yes
5	48	M	Pulmonary abscess	20 days	Chronic bronchitis	Gelfoam	No
6	41	M	Carcinoma	40 days	Chronic bronchitis	Gelfoam	No
				Lobectomy (56 Cases)			
1	38	F	Lipoid pneumonitis	5 wk.	Mild bronchitis	Areolar tissue	No
2	28	F	Bronchiectasis	6 wk.	Mild bronchitis	Areolar tissue	No

perhaps the most significant finding in the series with the pericardial fat graft, in addition to the low rate of bronchial fistulas, was the fact that the fat graft effectively protected the bronchus during the early vital weeks after pulmonary resection. In no instance in these 221 cases was there a fistula before the fourth week, the incidence of fistulas being twenty-two days, one month, six weeks, two months, and five months (Table V).

POST-MORTEM FINDINGS IN HUMAN BEINGS

We had ten post-mortem examinations in cases where the pericardial fat graft reinforcement was used. The deaths occurred in periods varying from the first postoperative day up to two years and nine months following operation (Table VI). In only one case was a bronchial fistula present. In this case, pneumonectomy for bronchiogenic carcinoma had been performed. The bronchial fistula occurred thirty-one days after pneumonectomy. The patient died of distant metastases one year after operation. On microscopic examination of the bronchial stump, the cause of the fistula was found to be due to residual carcinoma in the bronchial stump which, at operation, had appeared

TABLE V. ANALYSIS: BRONCHIAL FISTULA IN PERICARDIAL FAT GRAFT SERIES

	AGE	SEX	DIAGNOSIS	FISTULA	PATHOLOGY OF BRONCHUS	GRAFT BLOOD SUPPLY	CAUSE DEATH
				Pneumonectomy (118 Cases)			
1	58	M	Carcinoma	22 days 31 days	Undifferentiated carcinoma in bronchial stump	Poor	No
2	56	F	Carcinoma		Undifferentiated carcinoma in bronchial stump	Good	No
3	56	M	Pulmonary tuberculosis	2 mo.	Tuberculous bronchitis	Fair	No
4	68	M	Carcinoma	5 mo.	Bronchus normal. Fistula 5 mo. postempyema and wound disruption	Good	No
5	45	M	Bronchiectasis	2.5 mo.	Fistula 2½ mo. after empyema drainage	Good	No
				Lobectomy (113 Cases)			
6	58	M	Pulmonary tuberculosis	7 wk.	Fibrosing tuberculous bronchitis	Poor	No

TABLE VI. POST-MORTEM FINDINGS IN PULMONARY RESECTIONS WITH PEDICLE PERICARDIAL FAT GRAFT REINFORCEMENT OF BRONCHIAL STUMP

CASE	AGE	DIAGNOSIS	OPERATION	CAUSE OF DEATH	P.O. DAY	PATHOLOGIC FINDINGS
H.	72	Carcinoma	Pneumonectomy	Cardiac failure Pulmonary edema	1	Graft covers stump. No reaction to graft
N. G.	43	Pulmonary tuberculosis	Lobectomy	Pulmonary embolus	2	Graft fixed to stump. Leukocytic infiltration
J. V.	33	Pulmonary tuberculosis	Pneumonectomy	Tuberculous pneumonia	10	Graft firmly adherent. Leukocytic and fibroblastic infiltration of graft union
S.	51	Carcinoma	Pneumonectomy	Bronchopneumonia	17	Graft firmly fixed by adult connective tissue
L.	78	Lung abscess	Pneumonectomy	Bronchopneumonia	18	Similar findings to above
W. C.	66	Carcinoma	Pneumonectomy	Bronchopneumonia	30	Similar findings to above
F. M.	48	Carcinoma	Pneumonectomy	Coronary occlusion	39	See Fig. 20
D.	44	Carcinoma	Pneumonectomy	Metastatic carcinoma	5 mo.	See Figs. 19 and 21
N.T.	54	Carcinom	Pneumonectomy	Metastatic carcinoma	10 mo.	*Bronchial fistula* due to undetected cancer in bronchial stump
D.T.	65	Pulmonary tuberculosis	Pneumonectomy	Coronary occlusion	2 yr. 9 mo.	Fat graft viable adherent to stump by adult connective tissue

grossly normal. In the other nine cases, the pericardial fat graft was viable and tightly adherent to the bronchial stump in periods of from one day up to two years and nine months.

The gross appearance of a typical fat graft is shown on photograph at the post-mortem examination of a patient who died of metastatic carcinoma five months after pneumonectomy (Fig. 19). The microscopic findings are similar to those reported on the animal experiments. The same difficulty was encountered in cutting the microscopic sections, due to the fact that the tantalum wire sutures injured the microscopic section knives and these sutures had to be removed from the blocks before cutting. This resulted in considerable fraying of the material. However, leukocytic infiltration of the graft occurred early. Gradual replacement with fibroblasts and adult connective tissue of the portions of the bronchial wall and the adjacent graft tissue were noted. Outside the zone of fibrous adherence of the graft to the bronchial wall, the fatty tissue appeared healthy and a number of small blood vessels could be seen. The bronchial stump was completely lined with columnar epithelium in most instances, although occasionally a more transitional or cuboidal type of epithelium was seen. Some of the fat cells were phagocytosed and replaced with connective tissue, as observed in the experimental animals. However, the solid fibrous union of the graft in the wall of the major bronchus was clearly demonstrated (Figs. 20 and 21).

DISCUSSION

We have seen how the individual ligation technique for hilar structures for pneumonectomy,[25] lobectomy,[27] and segmental lobectomy[26] placed pulmonary resection on a sound anatomic basis. In closing the divided main bronchus following pneumonectomy, Rienhoff[25] first cut the cartilaginous rings of the bronchial stump at various points in their circumference in order to do away with a springlike action, which normally tends to maintain the

Fig. 19 (Case D).—Coronal section through trachea and coryna of a patient who died five months after left pneumonectomy for bronchiogenic carcinoma. Viable pedicled pericardial fat graft is fused to the bronchial stump. The graft has been invaded with carcinoma.

patency of the bronchus and is a major obstacle in bronchial closure. The bronchus was then sutured with interrupted silk sutures, the mucous membrane being approximated "as one would do in the suture of the mucous membrane elsewhere."

More recently, he[28] has advocated mattress sutures for the bronchial stump.[20] While Sweet[30] and others also emphasize preservation of the blood supply all the way to the cut end of the bronchus, approximating only the cut

Fig. 20.

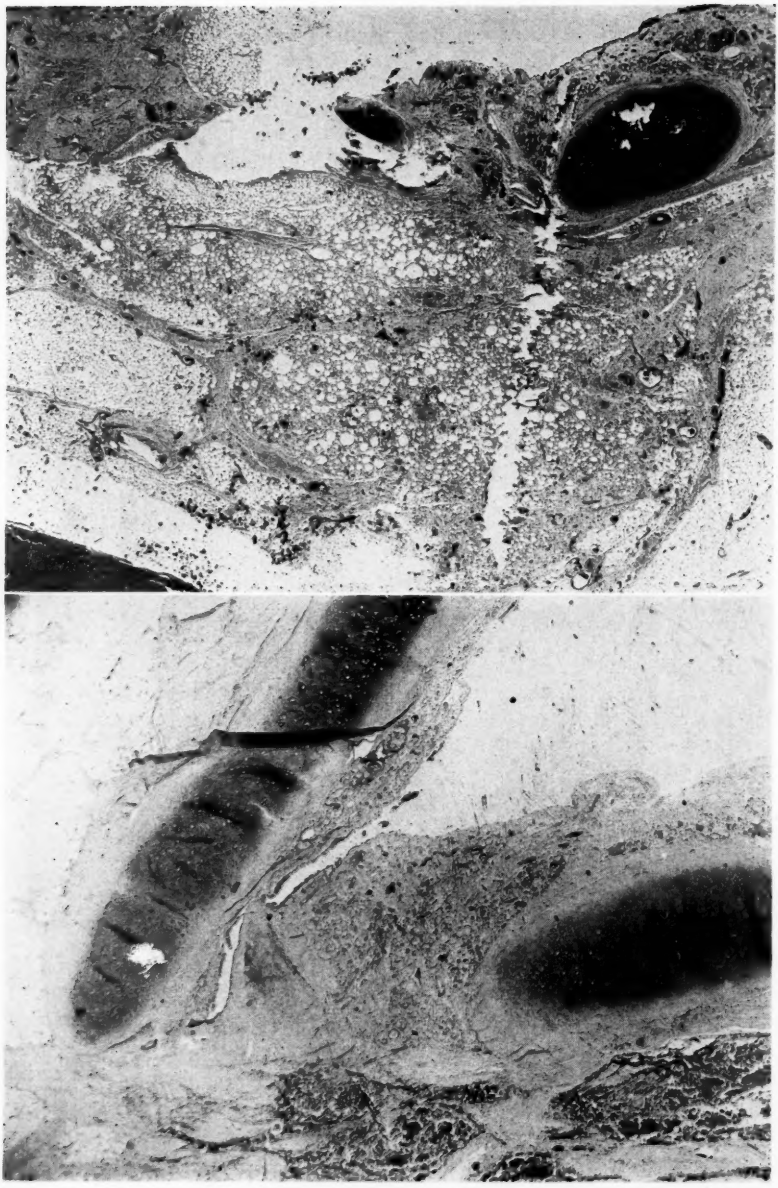


Fig. 21.

Fig. 20 (Case M).—Low-power microscopic section of bronchial stump taken from a patient who had a pneumonectomy for bronchiogenic carcinoma thirty-nine days before death. Section has been torn, in removing tantalum sutures, but viable fat graft is shown firmly united to bronchial wall by adult fibrous tissue. Note the blood vessel in lower left-hand corner.

Fig. 21 (Case D).—Low-power microscopic section of bronchial stump of Fig. 20 five months after pneumonectomy for bronchiogenic carcinoma. Fat graft seen in upper left corner of slide adherent to bronchial wall by fibrous tissue. Note recurrent carcinoma in lower left portion of section.

edges of the bronchus with simple sutures, they rely on a layer of pleura to reinforce the bronchial closure. Free grafts of lung tissue have been advocated for the bronchial stump by Churchill.[32] Peribronchial tissues have been drawn over the stump by Adams[33] and others, and Gelfoam has been advocated to reinforce the bronchial closure by Hanlon.[34]

Practically every type of suture material has been used for the bronchus. This includes silk (Rienhoff[28] and others), catgut (Shenstone and Janes[21]), a running stitch of silk (Holst[35]), cotton (Oschner[36]), stainless steel (Jones[37]), and tantalum wire (the authors).

In reviewing the results of pulmonary resection with the current techniques that have been mentioned for bronchial closure, a tremendous variation in the reported incidence of bronchial fistula is found. This variation ranges from 1 per cent[30] to as high as 40 per cent.[38] (This latter figure does include some tourniquet type of resection.) Perhaps, the average of reported incidence of bronchial fistula could be estimated as being from 8 to 15 per cent, although improvements in results are being reported. However, in reviewing these diverse reports in the literature, we find that there are many variables entailed in the compilation of such an average. These variables include the age of the patient, the amount and friability and infection of the bronchial wall, the use of antibiotics, the proper preparation of the patient, adequate postoperative care, etc. No two reports contain the same consideration of these variables. Thus, it becomes apparent that the assembling and mathematical calculation of such statistics from these widely divergent series (which was originally the plan) is not of true statistical value. We can conclude that while some people are not having much trouble with bronchial closure, in many reported series, bronchial closure is still an important clinical problem. We believe also that in nonreported series of cases, it is probably even more a clinical problem.

From this study, it can be concluded that sound surgical principles must be followed in closure of the bronchus to prevent the formation of a bronchopleural fistula following total pneumonectomy or lobectomy. In all of our cases, there was careful preparation of the patient to decrease bronchopulmonary infection and bronchial secretions. The importance of the proper antibiotic in addition to drainage procedures to minimize the bronchial infection cannot be stressed too much. During the operation constant aspiration of blood and secretions from the bronchial tree must be carried out even if the operation has to be sometimes considerably prolonged by this attention to the bronchial toilet. The better the preparation of the patient before surgery, the less trouble is encountered during and after surgery. The actual care of the bronchial stump must include the preservation of the blood supply up to the end of the stump, the avoidance of clamps and other trauma to the proximal end of the bronchus to be sutured, and the cutting of the bronchus in such a way as to avoid tension on the suture line. We feel that this is best effected by our method of making a small elliptical flap of the membranous portion of the bronchus, thus tension on the suture line is completely prevented. The actual suture of the bronchial stump is performed with simple

interrupted sutures that pass through the entire wall of the bronchus to firmly unite the mucosa. In most instances, the membranous flap is actually drawn over the rigid cartilaginous wall. The suture material is not as important as the manner in which it is used, since successful closures have been reported with fine absorbable and nonabsorbable sutures. However, since we've had such excellent results with tantalum wire, we will continue to use it. There seems to be general agreement that the bronchial stump should be covered by additional tissue. In our carefully controlled series of unselected cases, the viable pedicled pericardial fat graft proved greatly superior to all other methods. We must remember, however, that the use of antibiotics and pre- and postoperative care are extremely important. All of our cases have had liberal doses of vitamin C to promote healing following surgery.

The question remains, Should the pericardial fat graft be used routinely in all cases where the divided bronchial wall appears normal? Our experience with lobectomy in our two series does not show a great deal of improvement with the protecting influence of the graft, although the occurrence of late bronchial fistula was reduced from 2 per cent to 0.5 per cent. In pneumonectomy, however, there is no question that the graft should be used routinely for we had 5 per cent bronchial fistula before the first week, and three deaths directly due to these bronchopleural fistulas. With the grafts, however, there were no early bronchial fistulas before the fourth week and no deaths at any time from the opening of the bronchus. Thus, it is certain that the bronchial grafts are definitely indicated routinely in pneumonectomy and in all lobectomies where there is any question about the status of the bronchial wall or the effectiveness of the bronchial closure. Since it is extremely difficult to tell whether or not a bronchus is normal by gross inspection, this will leave only a few cases in which it is safe to omit the graft. Even though the occurrence of fistulas in lobectomy is rare, for any one patient that occurrence is 100 per cent. Because of this we shall continue to use this form of graft routinely in all cases.

SUMMARY

1. Our technique of bronchial closure, employing a curved posterior membranous flap which is sewn to the rigid cartilaginous wall of the main bronchus and the use of a viable, pedicled, pericardial fat graft reinforcement, has been presented.

2. The grafts of this "thoracic omentum" have been found to be intact, viable, and effectively reinforcing the bronchial stump one year after operation in experimental animals and up to 2 years and nine months in human beings on post-mortem examination.

3. Microscopic examination of the graft in experimental animals and human beings shows that first a leukocytic infiltration of the portion of the graft next to the stump, then the fibroblastic infiltration and replacement of portions of the graft next to the bronchus with an adult type of connective tissue. The bronchial stump is lined with columnar and occasionally low cu-

boidal or pavement epithelium. Portions of the graft not touching the bronchus show some fibrosis, but in general resemble pericardial fat tissue seen elsewhere in the body.

4. The bronchial reinforcement with the pericardial fat graft has entirely eliminated earlier bronchial fistulas during the first three weeks' time after operation in a series of 221 total pneumonectomies and lobectomies. Late bronchial fistulas occurred in 2.7 per cent of the cases. In an earlier series of 102 pulmonary resections in which the graft was not used, early bronchial fistulas were a real problem and made up four-fifths of the total number of fistulas. A total of 7.9 per cent of the patients developed bronchial fistulas in this nonfat graft series and three of the patients died as a result of the fistulas.

5. The employment of this technique of bronchial closure and pedicled viable pericardial fat graft reinforcement, as reported, appears to be a valuable addition to the surgery of pneumonectomy and pulmonary lobectomy.

6. A brief historical résumé of pulmonary resection and bronchial closure has been included.

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DISCUSSION

DR. RICHARD H. MEADE, Grand Rapids.—I think the authors have made a worthwhile contribution. I should like to ask if they have used this method in the treatment of bronchial fistulas.

DR. BREWER (Closing).—I can answer Dr. Meade's question very simply by saying that we have not used this method in the treatment of bronchial fistulas. All the bronchial fistulas in this series came on after three weeks' time and were treated by simple drainage. In all instances except one, where the patient had carcinoma in the bronchial stump, the bronchial fistula closed spontaneously following simple drainage.

I do believe that the pedicled pericardial fat graft can be used as an aid to close bronchial fistulas provided that (1) care is used to preserve the blood supply to the graft, and (2) adequate excision of the infected bronchial tissue is made. We have shown in experimental animals, in the incompletely closed bronchus, that fibroblasts proliferate in three days from the clean bronchial stump and by eight days the stump is epithelized when protected by the graft.

It seems reasonable, therefore, from this and from the examination of the firm fixation of the grafts seen at autopsy, that this method would be useful in closing bronchial fistulas.

This subject has been of consuming interest to our group. I gather from the lack of people springing to their feet to proclaim that they never heard of a bronchial fistula, that it is still a problem to most of us.

CIRCULATION THROUGH AN ATELECTATIC LUNG IN MAN

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STOCKHOLM, SWEDEN

IN AN experimental series performed using dogs, E. F. Salén and I studied the blood flow through an atelectatic lung with the aid of angiocardiography.

In an acute atelectasis of one lung the pulmonary arteries to that lung did not become smaller. The capillary bed remained open; this was indicated by the contrast medium's simultaneous filling of the pulmonary arteries and veins on both sides. The contrast filling of the periphery of the atelectatic lung was as little pronounced as on the other side. A pronounced decrease of the arterial oxygen saturation indicated a big shunt, that is, a considerable amount of blood passing the atelectatic lung.

In permanent atelectasis there was a continuous decrease of blood flow during the first month, until practically no blood was passing through the nonventilated part of the lungs. At the same time there was no decrease in the size of the main branches of the pulmonary artery.

In long-standing atelectasis the pulmonary artery decreased in size. After one month the diameter of the main pulmonary arteries, measured on the angiocardiogram, was 15 mm. on both sides. After eight months of atelectasis of the right lung the diameter of its main pulmonary artery measured 9 mm. as compared with a diameter of 15 mm. for the left pulmonary artery. The contrast medium did not disappear from the artery in the atelectatic lung in the same time as on the healthy side nor were the pulmonary veins filled with contrast medium in the atelectatic part at the same time as on the healthy side. The blood was therefore considered to fill the arteries of the atelectatic lung but either to pass not at all or to pass extremely slowly through the capillary bed.

Attempts to study the circulation through atelectatic lungs in man with angiocardiography have, however, not been successful so far. The density of the atelectatic lung with underlying disease in the clinical cases has made visualization of the finer branches of the pulmonary artery and veins impossible with contrast medium. In one patient who had more than one year's total atelectasis of the left lung only the main pulmonary artery on the left side was demonstrated. When all contrast had disappeared from the right pulmonary artery, the left branch to the atelectatic lung was still well demonstrated with high concentration of the contrast medium. This finding suggests a negligible circulation through the atelectatic lung. As no further information was obtained by angiography the following method was employed.

From the Sabbatsberg Hospital, Surgeon-in-chief: C. Crafoord.
Received for publication Feb. 9, 1953.

METHOD

For the determination of the blood flow to each lung separately Weiss, in 1926, used a formula necessitating the use of blood samples from a pulmonary vein both from the aerated and the collapsed lung as well as from the left ventricle. In an excellent experimental study Keeley and Gibson (1942) used this formula on dogs after having performed bilateral thoracotomies.

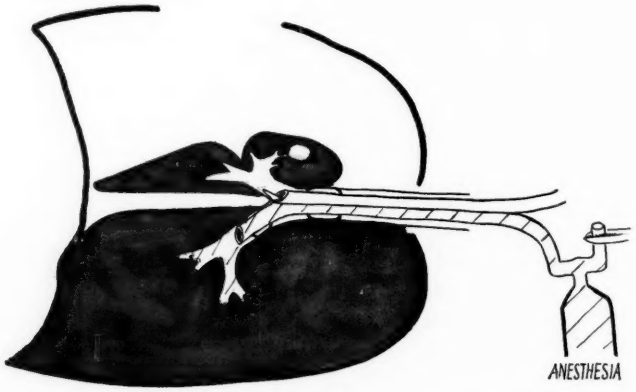

Fig. 1.—Acute atelectasis is obtained by the use of a double lumen catheter (Carlens). When the tube to the operated side is opened the lung will be completely atelectatic.

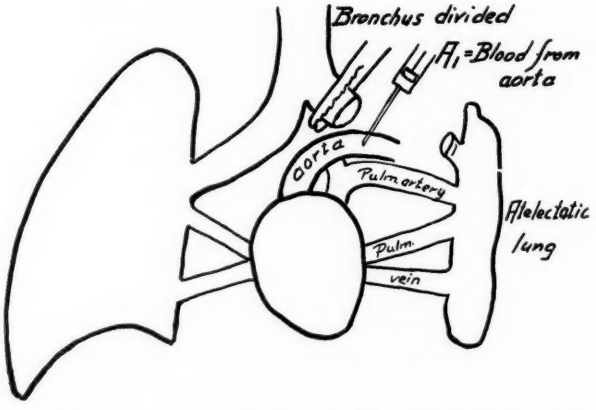

Fig. 2.—A_1 = blood from the aorta containing mixed blood from the aerated and from the atelectatic lung.

In order to make the determination of blood flow through an atelectatic lung possible on man I have worked out the following method: Acute atelectasis is obtained during intrathoracic surgery by the use of a double lumen catheter (Carlens) for endobronchial anesthesia. The tube, corresponding to the operated side, is opened to atmospheric pressure when the lung is completely atelectatic (Fig. 1). Anesthesia is then given only to the opposite lung. Nitrous oxide, oxygen, and curare has been the anesthesia of choice. After isolation of the pulmonary artery and veins and the bronchus, blood samples have

been taken for oxygen determination according to the method of Van Slyke and Neill. Double determinations of oxygen content as well as of oxygen capacity are made on each sample.

The blood samples are taken in the following order: 1. The first sample is from aorta (A_1). This sample contains mixed blood from the aerated and from the atelectatic lung (Fig. 2). 2. The second sample is from one pulmonary vein from the atelectatic lung (V). In case of lobar atelectasis samples are taken from both pulmonary veins. Before this sample is taken the vein is ligated or clamped as close to the pericardium as possible.

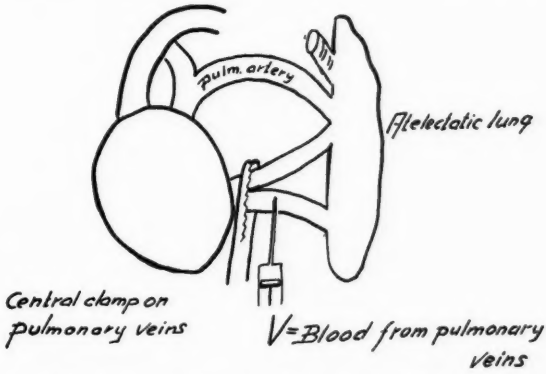

Fig. 3.—V = blood from the pulmonary veins draining the atelectatic lung.

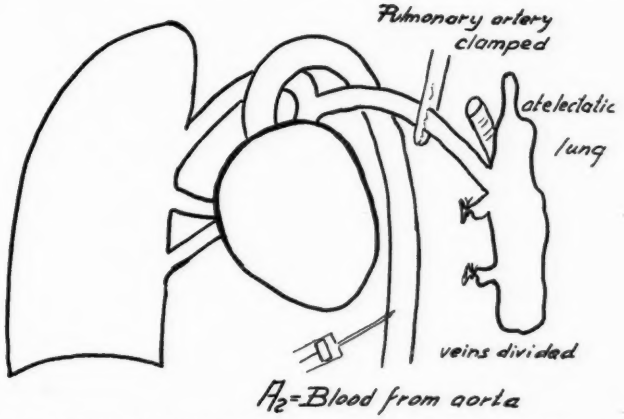

Fig. 4.—A_2 = blood from the aorta after the division or occlusion of the pulmonary veins from the atelectatic lung is identical to the blood from the pulmonary veins of the aerated lung.

Then the needle is introduced peripheral to the clamp. Thus a back-flow from the left auricle is eliminated. Immediately after the second sample is taken an arterial clamp is placed on the pulmonary artery to prevent the lobe or lung from being overloaded by blood (Fig. 3). 3. The third sample is from the aorta (A_2). This sample is taken after both the superior and inferior pulmonary veins are clamped or ligated. Even the pulmonary artery must be clamped in cases of acute atelectasis. The blood sample then represents the blood from the pulmonary veins on the opposite side, which without admix-

ing goes through the left auricle and ventricle and out in the aorta (Fig. 4). It is, however, necessary to wait a few minutes after ligation of both veins so that the mixed residual blood in the left ventricle is washed away. In our patient the third sample (A_2) was taken immediately after ligation of both upper and lower pulmonary veins, and the arterial oxygen content was 95.9 per cent in a case of one hour's atelectasis. Another sample, taken two minutes later from the same patient's aorta, showed an arterial oxygen content of 99.2 per cent.

Calculation.—x represents the percentage of total pulmonary blood flow through the aerated lung. y represents the percentage of total pulmonary blood flow through the atelectatic lung. $x + y = 100$ per cent of the pulmonary blood flow. $y = 100 - x$. Then the following equation is achieved:

$$A_2x + Vy = A_1 (x + y)$$
$$y = 100 - x$$
$$A_2x + 100V - Vx = 100\ A_1$$
$$x(A_2 - V) = 100\ (A_1 - V)$$
$$x = \frac{100\ (A_1 - V)}{A_2 - V}$$

In cases of chronic atelectasis the blood flow through the opened pulmonary veins with intact pulmonary artery and divided bronchial arteries was measured during operation (Fig. 5). These observed values of blood flow were compared to the values calculated from the above-mentioned formula. See Tables I and II.

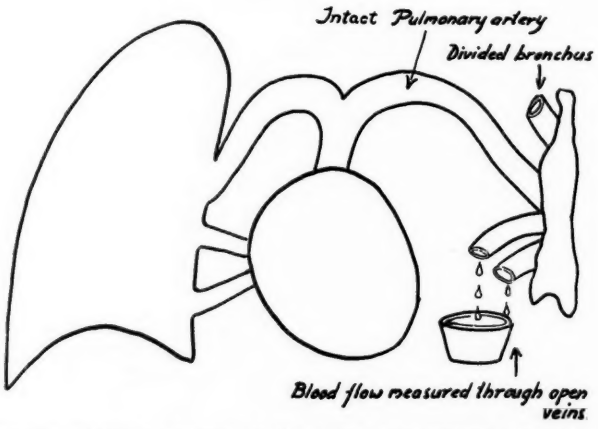

Fig. 5.—In cases of chronic atelectasis the blood flow was measured through the open veins when the pulmonary artery was intact and the bronchial arteries divided.

The Influence of the Bronchial Circulation.—It has been my intention to study the circulation through the pulmonary artery separately without the admixture of blood from the bronchial arteries. In bronchiectases and in many cases of pulmonary tuberculosis the bronchial circulation is considerable, but in tuberculosis with bronchial stenosis and total atelectasis only small bronchial arteries are usually found at the operation. In acute atelectasis the admixture of blood from the bronchial arteries would hardly influence the result, as the volume of flow through the pulmonary artery is so much greater. In chronic atelectasis, however, where the flow through the pulmonary artery is negligible, an admixture of blood from the bronchial artery must be excluded. Furthermore in atelectatic lungs with bronchiectatic changes there are much larger anastomoses between the bronchial and pulmonary arteries than in normal cases. Only sample A_1 and V would be influenced

TABLE I. TOTAL ATELECTASIS OR DESTROYED LUNGS

AGE	SEX	DIAGNOSIS	DURATION OF ATELECTASIS	A_1		A_2		V		P		CALCULATED FLOW THROUGH DISEASED LUNG IN % OF TOTAL FLOW	OBSERVED BLOOD FLOW THROUGH OPEN VEINS IN ML./MIN.	COMMENTS
				O_2	CO_2	O_2	CO_2	O_2	CO_2	O_2	CO_2			
30	F	TBC stenosis left main bronchus	2 yr.	100.0	51.4	100.0	52.8	68.6	49.1	—	—	0	420	Probably accumulation of blood as veins were clamped 15 minutes before they were opened
46	F	Total atelectasis. Left lung with fibrosis	9 mo.	100.0	38.3	—	—	—	—	—	—	—	0	
48	F	TBC stenosis of left upper and lower lobe bronchi. 7 ribs thoracoplasty 2 years ago	2 mo.	87.3	56.7	88.2	53.8	60.8	56.8	—	—	3.3	90	Bronchial arteries not divided
29	F	Destroyed lung. Bronchiectasis	23 yr.	94.6	52.1	93.2	50.4	51.0	54.9	59.0	54.4	0	—	
25	M	TBC with atelectasis under 6-rib thoracoplasty	6 yr.	67.0	48.7	65.0	48.9	52.0	48.2	48.2	50.0	0	—	Bronchospirometry showed 0% oxygen uptake on the left side
33	F	TBC stenosis left main bronchus and pneumothorax	8 yr.	99.4	49.3	100.0	48.2	77.3	—	86.2	50.8	2.7	—	
31	M	TBC stenosis left main bronchus	3 yr.	76.4	46.8	86.1	47.2	35.4	51.3	58.3	50.1	19.0	34	
44	F	TBC stenosis left main bronchus. 7-rib thoracoplasty	9 yr.	89.2	43.7	87.8	43.3	55.6	44.8	68.2	45.6	0	80	
27	F	TBC empyema left side and 7-rib thoracoplasty	2 yr.	96.4	46.7	100.0	47.3	57.6	52.0	65.7	50.8	8.5	50	Bronchospirometry showed 0% oxygen uptake on the left side
30	F	TBC stenosis left main bronchus	5 yr.	—	—	—	—	—	—	—	—	—	28	
33	M	TBC stenosis left main bronchus and pneumothorax	3 yr.	100.0	48.4	85.0	42.5	66.4	43.2	81.8	44.4	0	84	
		Mean Value:		91.0	47.6	89.5	48.3	58.3	50.1	66.7	49.4	0	98.3	

A_1 = blood from aorta before occlusion of the veins.
A_2 = blood from the aorta after occlusion of the pulmonary veins.
V = blood from the pulmonary veins.
P = blood from pulmonary artery.

TABLE II. CASES WITH TOTAL ATELECTASIS OF LEFT UPPER LOBE, RELATIVE MAIN BRONCHUS STENOSIS, AND HYPERINFLATION OF EMPHYSEMATOUS LOWER LOBE

AGE	SEX	DIAGNOSIS	DURATION OF ATELECTASIS IN YEARS	A_1		A_2		$V_{sup.}$		$V_{inf.}$		P		CALCULATED FLOW THROUGH DISEASED UPPER LOBE IN % TOTAL FLOW	BLOOD FLOW THROUGH OPEN	
				O_2	CO_2	O_2	CO_2	O_2	CO_2	O_2	CO_2	O_2	CO_2		SUP. PULM. VEIN ML./MIN.	INF. PULM. VEIN ML./MIN.
32	M	TBC stenosis left upper lobe. Relative main bronchus stenosis	3	94.4	50.3	96.8	50.7	67.9	53.6	97.1	47.6	69.4	54.4	7.7	33.0	171
49	M	TBC stenosis left main bronchus hyperinflated over lobe	8	95.9	49.3	97.3	50.6	90.7	50.3	67.7	52.0	80.5	51.1	4.7	41.0	65
38	F	TBC stenosis left upper lobe. Hyperinflation lower lobe	4	100.0	50.9	93.6	48.0	69.2	53.3	79.1	54.8	79.5	53.4	0	32.0	156
48	F	TBC stenosis left upper lobe. Relative stenosis left lower lobe with hyperinflation 7-rib thoracoplasty	3	100.0	45.5	100.0	45.0	84.6	43.7	83.9	42.9	82.9	45.9	0	43.5	360
		Mean Values		97.6	49.0	96.9	48.6	78.1	50.2	82.0	49.3	78.1	51.2	0	37.4	188

Blood from: A_1 = aorta before occlusion of veins.
A_2 = aorta after occlusion of veins.
$V_{sup.}$ = superior pulmonary vein.
$V_{inf.}$ = inferior pulmonary vein.
P = the pulmonary artery.

by the bronchial circulation, which is drained into the pulmonary veins as well as through the intercostal, the azygos, and hemiazygos veins into the superior vena cava. When sample A_2 is taken, both pulmonary veins are clamped or ligated to exclude admixture from the bronchial circulation. To exclude bronchial circulation in chronic atelectasis where the lung is going to be removed, all bronchial arteries are tied and the bronchus is divided. In cases where an acute atelectasis is produced and only part of the lung or a mediastinal tumor is removed, the main bronchus is dissected and clamped together with the bronchial arteries with the noncrushing aorta clamp constructed by Crafoord. This technique is used to produce a bloodless field in the enucleation resections of benign intrapulmonary tumors. In patients with acute atelectasis an abnormal bronchial artery joining the lung peripheral to the clamped bronchus may be encountered, but this admixture will not significantly influence the values of flow through the pulmonary artery.

Criticism of the Method.—The limitation of this method lies in the oxygen saturation determination. Due to the form of the oxyhemoglobin dissociation curve, which is very flat at high tensions, small changes in the arterial-oxygen content may not be detected with the saturation determination. From a theoretical point of view arterial oxygen tension determinations are therefore preferred. Direct oxygen tension measurements, however, have not been performed during operations due to the admixture of nitrous oxide to the blood.

ACUTE ATELECTASIS OF ONE HOUR'S DURATION

Acute atelectasis of the right lung was produced in two cases during operation.

CASE 1.—A 59-year-old man had a segmental atelectasis of the posterior segment of the right upper lobe due to a squamous-cell bronchiogenic carcinoma.

CASE 2.—A 23-year-old woman had a tuberculous cavity in the apical segment of the right lower lobe. The determination was made after resection of the diseased segment.

The duration of the total atelectasis of the right lung was one hour in both instances. The values shown in Tables III and IV were obtained.

TABLE III. ACUTE ATELECTASIS FOR ONE HOUR OF THE RIGHT LUNG

	A_1		V		A_2		BLOOD FLOW	
	% O_2	VOL. % CO_2	% O_2	VOL. % CO_2	% O_2	VOL. % CO_2	RIGHT LUNG	LEFT LUNG
Case 1	81.6	48.1	62.8	49.9	99.2	46.0	48.4%	51.6%
Case 2	87.0	42.4	70.0	40.7	99.5	36.0	42.4%	57.6%

A_1 = blood sample from aorta.
V = blood sample from the right pulmonary veins.
A_2 = blood sample from aorta after division of the right pulmonary veins.

TABLE IV. BRONCHOSPIROMETRY IN CASE 2

	RIGHT LUNG	LEFT LUNG
Minute ventilation	46.5%	53.5%
Oxygen uptake	37.8%	62.2%

Conclusion.—In both cases the right lung had been atelectatic for one hour. In the first case, where the posterior segment of the right upper lobe was diseased, 48.4 per cent of the total blood flow through the lungs passed the atelectatic right lung. This may be considered to be about the normal proportion of blood flow through the lungs in spite of atelectasis for one hour of the right lung.

In Case 2 the blood samples were taken after the apical segment of the right lower lobe was removed. This segment is usually larger than the posterior segment of the upper lobe. The finding that 42.4 per cent of the total blood flow was passing the right lung after atelectasis for one hour is considered to correspond to normal proportion. When the patient underwent a bronchospirometry one year after the operation the oxygen uptake on the right side was found to be 37.8 per cent (the minute ventilation on the right side was 46.5 per cent). The oxygen uptake of each lung is considered to be a good expression for the blood flow through each lung.

Therefore the conclusion that can be drawn from these two cases is that after one hour of total atelectasis a normal amount of blood is still passing the atelectatic lung.

ATELECTASIS FOR ONE AND ONE-HALF MONTHS

A 22-year-old girl had a left lower lobe bronchial stenosis of tuberculous origin and a long-standing lower lobe atelectasis. The upper lobe was well aerated under the artificial pneumothorax. After a first-stage upper 5-rib thoracoplasty the upper lobe, too, was atelectatic for one and one-half months. Then a left lower lobectomy and decortication of the upper lobe was performed. At the end of the operation the blood flow through the remaining left upper lobe that had been atelectatic for one and one-half months was found to be negligible. The following values were obtained:

SAMPLES	O_2 SATURATION
A_1 (aorta before occlusion of V)	= 98.5% O_2
V (left upper pulmonary vein)	= 60.0% O_2
A_2 (aorta after occlusion of V)	= 91.0% O_2

The upper lobe had been atelectatic for one and one-half months. Now it was ventilating. However, the calculated flow through this lobe equaled zero. One year after the resection this patient underwent a bronchospirometry which showed 15.7 per cent oxygen uptake and 28 per cent minute ventilation for the remaining left upper lobe. Thus the same function was achieved that had existed before the atelectasis when the oxygen uptake of left upper lobe was 14.3 per cent and the minute ventilation 27 per cent of the total.

Conclusion.—After atelectasis for one and one-half months no blood passed this left upper lobe in spite of decortication and positive pressure ventilation. Bronchospirometry one year later showed 15.7 per cent oxygen uptake and 28 per cent minute ventilation for this remaining left upper lobe. Exactly the same function had then returned as was found before the atelectasis (oxygen uptake 14.3 per cent and minute ventilation 27 per cent).

CHRONIC ATELECTASIS

The same decrease of blood flow was found in a destroyed lung due to bronchiectasis as was found in cases of tuberculosis with or without bronchial stenosis.

The Main Pulmonary Artery.—The size of the main pulmonary artery showed great variations. In four cases the pulmonary artery had a normal size in spite of total atelectasis which had been present for one to three years. In three cases the pulmonary artery had a nearly normal size 70 mm. in spite of the fact that the lung was completely collapsed for nine years.

In two cases the pulmonary artery had considerably diminished in size. The circumference was only 35 to 40 mm., approximately half the size of the normal artery. The duration of the atelectasis was twenty-three and eight years, respectively. In the remaining six cases a varying decrease of the size of the pulmonary artery was found.

Conclusion.—In cases of chronic atelectasis the main pulmonary artery may for many years retain its normal size. The pulmonary artery is then only functioning as a blind sac with a negligible amount of blood flow (probably in a reverse direction) through the destroyed lung. After several years the pulmonary artery to the destroyed lung slowly diminishes in size. The most pronounced decrease observed was about 50 per cent.

The Branches of the Pulmonary Artery.—The peripheral branches of the pulmonary artery to a diseased area are often diminished in size. We have encountered complete thromboses of the anterior trunk to the right upper lobe, the lingular artery, and the artery to the apical segment of the left lower lobe in cases of tuberculosis.

The Pulmonary Veins.—The pulmonary veins of the lungs having long-standing atelectasis are nearly always considerably diminished in size.

The Bronchial Arteries.—In cases of chronic atelectasis due to tuberculosis great variation is found in the bronchial arteries. They are often very small, but considerably enlarged bronchial arteries may occasionally be found. In tuberculosis the bronchial arteries have never been found as large as in cases of bronchiectasis. Eleven cases of long-standing total atelectasis were investigated. The results can be seen in Table I.

CONCLUSIONS

In cases with total atelectasis or a destroyed lung the following observations were made:

1. The oxygen saturation in the aorta was on an average the same before (91.0 per cent) and after (89.5 per cent) the occlusion of the pulmonary veins from the diseased lung.

2. The amount of blood flowing through the diseased lung was 0 per cent, calculated from the mean values.

3. The amount of blood flowing through the diseased lung observed during operation was on an average 98 ml. per minute.

4. The mean value of the oxygen saturation in the pulmonary artery (66.7 per cent oxygen) was significantly higher than in the pulmonary veins (58.3 per cent oxygen). This may be due to an admixture of blood from the bronchial arteries draining blood into the pulmonary artery in a reverse direction.

5. In cases of total atelectasis only a negligible amount of blood passes the pulmonary artery. Thus the pulmonary artery is probably acting more or less as a blind sac with a slow reverse flow of blood from the bronchial arteries. In four cases with total atelectasis of the left upper lobe and a relative stenosis of the main bronchus of the lower lobe with hyperinflation of an emphysematous lower lobe the observations demonstrated in Table II were made.

In cases of total atelectasis of the left upper lobe and hyperinflation of the emphysematous lower lobe the following findings were made:

1. The oxygen saturation, in the aorta, was on an average the same before (97.6 per cent oxygen) as after (96.9 per cent oxygen) occlusion of the pulmonary veins from the diseased lung.

2. The amount of blood flowing through the diseased lung was calculated to 0 per cent on the mean values.

3. The amount of blood flowing through the atelectatic lobe (37.4 ml. per minute) was considerably smaller than the amount passing the hyperinflated lobe (188 ml. per minute).

4. The mean oxygen saturation in the pulmonary artery (78.1 per cent) was the same as in the superior pulmonary vein (78.1 per cent) but slightly higher in the inferior pulmonary vein (82 per cent).

SUMMARY

A method is presented for the determination of the relative blood flow through each lung during intrathoracic operations on man.

The values obtained correspond well to the direct measurement of blood flow through the opened pulmonary veins when the pulmonary artery is intact in cases of chronic atelectasis or destroyed lungs.

Acute atelectasis for one hour does not significantly decrease the blood flow through the atelectatic lung in man. After atelectasis for one and one-half months practically no blood was passing through the atelectatic lung. One year later the oxygen uptake on that lobe was 15.7 per cent.

In cases of chronic atelectasis or destroyed lungs a negligible amount of blood passes through the diseased lungs. A higher oxygen saturation in the pulmonary artery than in the pulmonary veins suggests a reverse blood flow in the pulmonary artery with an admixture of blood from the bronchial arteries. In these chronic cases the amount of unsaturated blood leaving the pulmonary veins is too small to cause a decrease in the oxygen saturation of the arterial blood.

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RESECTION OF MULTIPLE PULMONARY METASTASES FOURTEEN YEARS AFTER AMPUTATION FOR OSTEOCHONDROGENIC SARCOMA OF TIBIA

Apparent Freedom From Recurrence Two Years Later

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ALTHOUGH there have been reported only a few patients with metastatic pulmonary neoplasms of osseous origin who have been treated by pulmonary resection, it is noteworthy that some excellent results have been obtained in this group. As early as 1883, Krönlein[1] removed a metastatic sarcoma in the left lower lobe; the patient lived for six years after the operation, dying of a recurrence of the primary neoplasm of the rib but without evidence of further pulmonary metastasis. One of Van Hazel's[2] patients was alive nine years after a left upper lobectomy for a metastatic osteogenic sarcoma. An even more striking case was that described by Edwards[3] whose patient was alive eighteen years following pulmonary resection for a metastatic sarcoma of the fibula. The only reported case of pulmonary resection for multiple metastatic neoplasms of osseous origin of which we have knowledge is that described by Weinlechner.[4] This patient died in the early postoperative period.

In the case described here, a total of six metastatic neoplasms was discovered in the left lung during exploratory thoracotomy. Prior to operation only one tumor was seen roentgenographically. All the palpable lesions were resected, and the patient, previously suffering from chest pain and hemoptysis, has been symptom free and without evidence of recurrence for twenty-four months following operation.

CASE REPORT

B. H., a 39-year-old white woman, was admitted to the University of Michigan Hospital (Reg. No. 666306) on Oct. 26, 1950. Fourteen years previously a left midthigh amputation had been performed for an osteochondrogenic sarcoma of the tibia (Fig. 1); chest roentgenograms showed no abnormality. In 1949, she developed pain in the left chest, night sweats, productive cough, and hemoptysis. At that time there was found in the roentgenogram of the chest a solitary opacity which was considered to be a tuberculoma. In view of a persistence of symptoms and slight enlargement of the lesion during the succeeding year, exploratory thoracotomy was advised.

At the time of admission the only abnormal sign was an unexplained tenderness over the amputation stump and along the left side of the chest. The bronchoscopic findings, laboratory data, and roentgenogram of the femoral stump were negative.

At operation on Nov. 3, 1950, six metastases were found in the left lung (Fig. 2). The largest of these, a firm ovoid mass 20 mm. in diameter, was the only lesion seen in the roentgenogram before operation and was one of five lesions located in the basilar segments of the left lower lobe. These tumors were removed by basilar segmentectomy. The sixth and smallest nodule was found on the anterior surface of the lingula and was resected locally.

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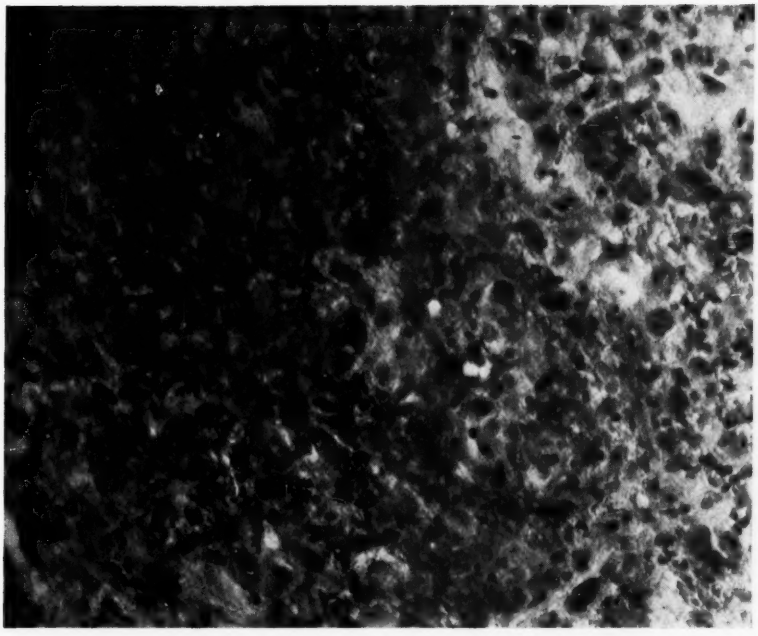
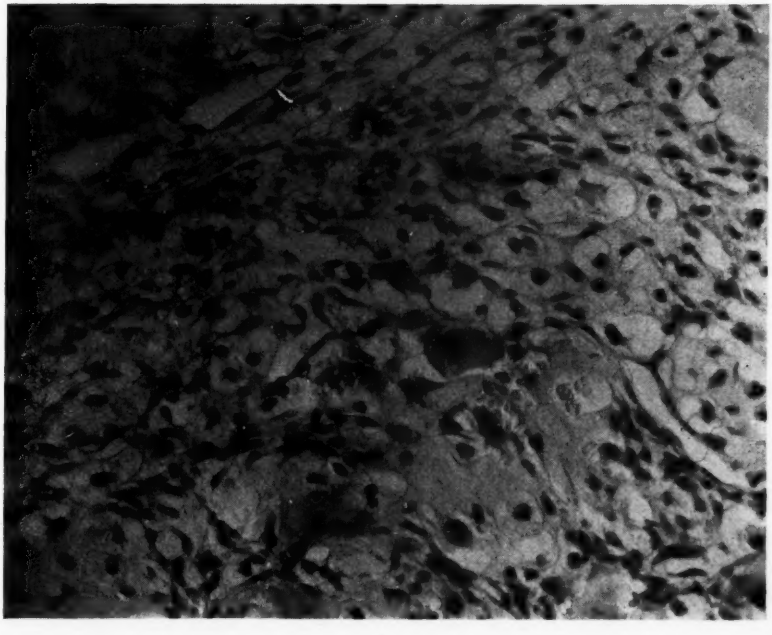


A.



B.

Fig. 1.—Photomicrographs of the original osteochondrogenic sarcoma of the tibia. *A*, A highly anaplastic area with many prominent nuclei and nucleoli. *B*, Cartilaginous elements with scattered areas of telangiectasis predominate in this section.

The procedure was well tolerated and the postoperative course was uneventful. It is now twenty-four months since the operation. The patient has no symptoms, and lateral and posteroanterior roentgenograms of the chest are normal.

Histologically the lesions were described as cellular osteochondromata, metastatic to the lung.

DISCUSSION

Pathology.—The original neoplasm was a vascular osteochondrogenic sarcoma (Fig. 1, *A* and *B*). Geschickter[5] states that the five-year survival rate in primary chondrosarcoma is 15 per cent. Inasmuch as there is at present no evidence of the existence of neoplasm in the amputation stump or elsewhere in the body, it seems probable that the pulmonary neoplasms were present prior to the amputation of the thigh. It may be that the local tissue resistance of the lung to the growth of neoplasms, as recently mentioned by Sommer,[6] was a factor in their occasional suppression for so long a time. Metastatic pulmonary neoplasms are a threat to the patient not only because of their local effect in the lung, but also because they may act as sources of systemic embolization.

Fig. 2.—A low-power view of one of the metastatic pulmonary osteochondromata.

According to Jaffe,[7] osteochondrogenic sarcoma tends to metastasize to only one lung more often than osteogenic sarcoma from which the spread is so often bilateral. This observation, if confirmed, is obviously of considerable prognostic significance. The metastatic neoplasms in our case appeared microscopically less malignant than the original lesion, but the possibility that they might be

chondromata arising primarily in the lung, as described by Virchow,[8] is considered very unlikely. In support of this opinion were the multiplicity of the lesions, the peripheral location of several of the nodules, the relative rarity of multiple primary osteochondromata in the lungs, and the similarity of the metastases to some of the less malignant areas in the original neoplasm (Fig. 2).

Fig. 3.—A rounded shadow is seen just anterior to a vertebral body and superior to the left hemidiaphragm. This proved to be the largest of the six metastatic lesions.

Roentgenology.—The importance of periodically obtaining lateral as well as posteroanterior roentgenograms after the removal of primary neoplasms is emphasized by the fact that even the largest of the metastases in our case did not appear roentgenographically until thirteen years after operation, and then it was visible only in the lateral view (Fig. 3). The radiopaque density within the neoplasm (Fig. 4) led originally to an erroneous diagnosis of a tuberculoma with calcification. In retrospect, the validity of this opinion might well have been questioned because of the history of an amputation having been performed previously for osteochondrogenic sarcoma of the tibia and because of the fact that the deposition of calcium is a nonspecific change which may occur in tissues which are the site of degenerative or inflammatory, as well as neoplastic, changes.[9, 10]

The roentgen detection of small pulmonary neoplasms presents a problem. Rigler[11] states that when favorably situated metastases as small as 2 mm. in diameter have been diagnosed but that small subpleural metastases, which have been demonstrated at autopsy later, have not often been apparent radiologically.

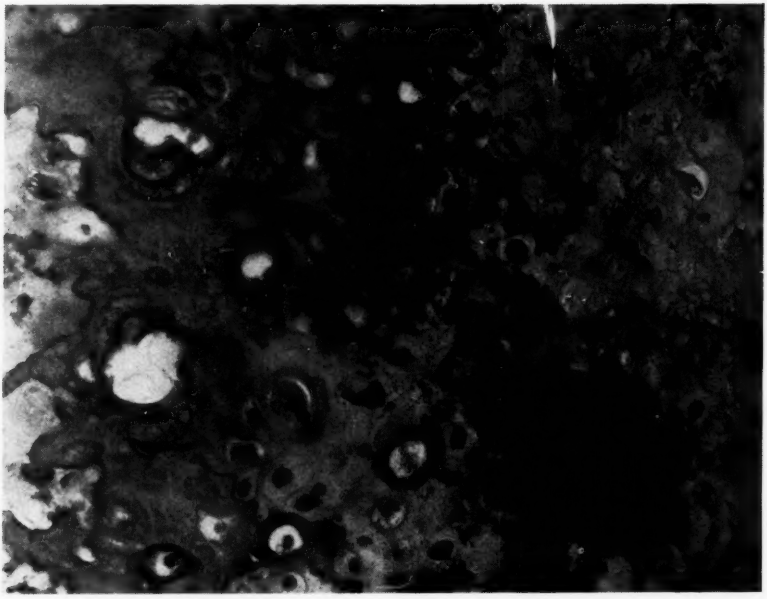


Fig. 4.—A microphotograph of a section through the radiopaque density seen near the center of the tumor shown in Fig. 3.

In our case, when the preoperative planigrams (made at 2 cm. distance from one another) were reviewed after operation, a second neoplasm was detected for the first time. The other four lesions were not discernible in the planigrams, although the smallest lesion found in the lung at operation measured 4 mm. in diameter.

Treatment.—The only specific reference to a plan of treatment for multiple metastatic neoplasms of which we have knowledge is that of Minor.[12] He advised that the pulmonary lesions should be resected without delay in any patient whose primary lesion had been successfully treated and who had one or more pulmonary metastases so located that they could be resected without removing more than the volume of one lung, and who had no discoverable extrapulmonary metastases. The unexpected discovery at the operation table of six neoplasms instead of one, led to some discussion as to the best course of action in our case. Some of the surgeons felt that the multiplicity of lesions was in all probability indicative of a generalized "seeding" with metastases as yet undiscovered, and that, therefore, resection was not indicated. Also in defense of this opinion was the slowness of growth of the neoplasms already discovered, and the consequent hope that many more years would pass before death.

Resection of the tumors in our case was decided upon because: 1. There was virtually no hope for cure if the metastases were not removed. 2. The patient was a young woman with an otherwise long life expectancy, and for whom the operative risk was small. 3. The results obtained in the treatment of solitary pulmonary metastases of various types (especially sarcoma) have been so encouraging in selected cases that an aggressive policy in regard to multiple metastases seemed warranted. In this respect, fear of the likelihood of the later appearance of pulmonary or other metastases should not necessarily deter the surgeon from resection. A patient described by Alexander and Haight[13] was free of recurrence twelve years following bilateral pulmonary resections for metastases. 4. The metastases in our case apparently were the cause of pleuritic pain and hemoptysis. These symptoms disappeared after the resection. Seiler and his associates[14] felt that palliative resection for metastatic malignant lesions was occasionally justified. 5. The rare possibility of multiple primary neoplasms of the lung could not be excluded.

Prognosis.—Although the appearance of additional metastases in the lungs or elsewhere is a definite possibility in our patient, especially in view of the microscopic appearance of low-grade malignancy, their not having done so in the two years since the thoracic operation is obviously a hopeful sign.

SUMMARY AND CONCLUSIONS

1. A case is reported in which six metastatic osteochondrosarcomata were removed from one lung fourteen years after a midthigh amputation for osteochondrogenic sarcoma of the tibia.

2. The patient has been freed of symptoms, and no recurrence has appeared since the pulmonary resections; these were done twenty-four months ago.

3. In selected cases a more aggressive attitude than heretofore employed may be indicated in the treatment of multiple metastatic pulmonary neoplasms.

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Announcement

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The 34th annual meeting of the American Association for Thoracic Surgery will be held May 3, 4, and 5, 1954, in Montreal, Que., Canada. Headquarters will be at the Sheraton-Mount Royal Hotel.

Requests for Hotel Reservations

These should be mailed *directly* to the Reservation Manager, Sheraton-Mount Royal Hotel, Montreal, Que., Canada. Please mention this Association, type of accommodation desired, date, and approximate hour of arrival. If accommodations are desired elsewhere, please communicate directly with hotel of your choice.

Thoracic Surgical Forum

After due consideration, the Council has decided to try an experiment by assigning one morning session to a "Thoracic Surgical Forum" for the presentation of short papers on current thoracic research, anatomy, modified surgical techniques, etc. Papers at this session will be limited sharply to ten minutes (including the showing of lantern slides or other illustrative material) with three minutes as the maximum discussion of each paper.

These papers will be published together in one issue of THE JOURNAL OF THORACIC SURGERY. Maximum length: 3,000 words without illustrations. If illustrated, an appropriate number of words must be subtracted for each cut used.

Abstracts for Papers

Abstracts for the presentation of papers at the 1954 meeting, including papers before the Forum, must be received on or before January 1, 1954, otherwise they will not be considered by the Program Committee.

Abstracts should be labeled "For Forum" or "For Regular Program."

Five, repeat five, copies of each abstract should be sent to the Secretary of the Association, Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif. They should not be sent to the Editor.

The abstracts should contain from 200 to 250 words and accurately reflect the contents of the completed paper.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee not later than Jan. 1, 1954, to be considered for action in Montreal. Applications received beyond this deadline will be deferred for consideration until 1955.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the sponsoring statement on the application form, the sponsors *must* submit a separate letter concerning the applicant direct to Dr. Lyman H. Brewer, III, Chairman of the Membership Committee, 2010 Wilshire Blvd., Los Angeles, Calif. Completed application forms should likewise be sent to Dr. Brewer. These regulations are at the direction of the Council and were made effective in 1952 at Dallas.